4/28/05

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|---|---|---|---|
| NEWS | 1 | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS | 2 | | "Ask CAS" for self-help around the clock |
| NEWS | 3 | FEB 25 | CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered |
| NEWS | 4 | FEB 28 | PATDPAFULL - New display fields provide for legal status data from INPADOC |
| NEWS | 5 | FEB 28 | BABS - Current-awareness alerts (SDIs) available |
| NEWS | 6 | FEB 28 | MEDLINE/LMEDLINE reloaded |
| NEWS | 7 | MAR 02 | GBFULL: New full-text patent database on STN |
| NEWS | 8 | MAR 03 | REGISTRY/ZREGISTRY - Sequence annotations enhanced |
| NEWS | 9 | MAR 03 | MEDLINE file segment of TOXCENTER reloaded |
| NEWS | 10 | MAR 22 | KOREAPAT now updated monthly; patent information enhanced |
| NEWS | 11 | MAR 22 | Original IDE display format returns to REGISTRY/ZREGISTRY |
| NEWS | 12 | MAR 22 | PATDPASPC - New patent database available |
| NEWS | 13 | MAR 22 | REGISTRY/ZREGISTRY enhanced with experimental property tags |
| NEWS | 14 | APR 04 | EPFULL enhanced with additional patent information and new fields |
| NEWS | 15 | APR 04 | EMBASE - Database reloaded and enhanced |
| NEWS | 16 | APR 18 | New CAS Information Use Policies available online |
| NEWS | 17 | APR 25 | Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications. |
| NEWS | 18 | APR 28 | Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus |

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

| | |
|---|---|
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| NEWS LOGIN | Welcome Banner and News Items |
| NEWS PHONE | Direct Dial and Telecommunication Network Access to STN |
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FILE 'HOME' ENTERED AT 13:06:12 ON 28 APR 2005

=> file registry
COST IN U.S. DOLLARS

| | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 13:06:22 ON 28 APR 2005
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STRUCTURE FILE UPDATES: 27 APR 2005 HIGHEST RN 849400-77-7
DICTIONARY FILE UPDATES: 27 APR 2005 HIGHEST RN 849400-77-7

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**********
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
**********

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10810649-2.str

L1 STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 13:06:57 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 28916 TO ITERATE

3.5% PROCESSED 1000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

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FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       568153 TO   588487
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 13:07:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 574251 TO ITERATE

 69.7% PROCESSED  400000 ITERATIONS                                70 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.08

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                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       574251 TO   574251
PROJECTED ANSWERS:              70 TO      130

L3           70 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             161.76     161.97

FILE 'CAPLUS' ENTERED AT 13:07:20 ON 28 APR 2005
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FILE COVERS 1907 - 28 Apr 2005  VOL 142 ISS 18
FILE LAST UPDATED: 27 Apr 2005  (20050427/ED)

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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s l3
L4           27 L3

=> d abs bib fhitstr 1-27

L4   ANSWER 1 OF 27  CAPLUS  COPYRIGHT 2005 ACS on STN
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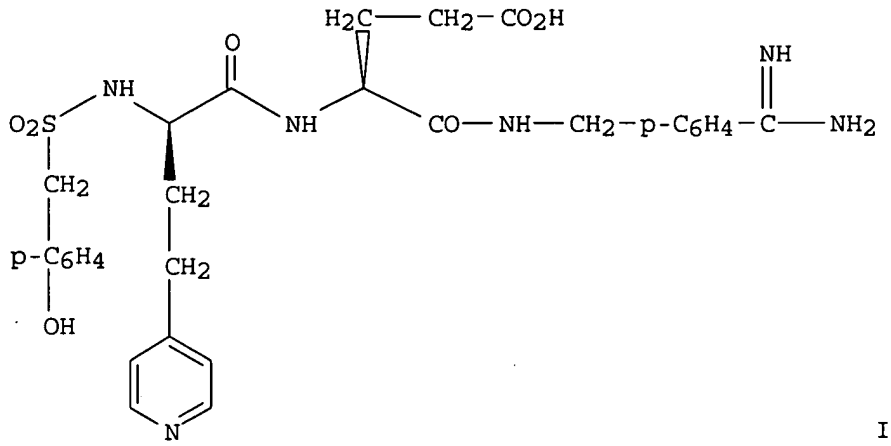
GI



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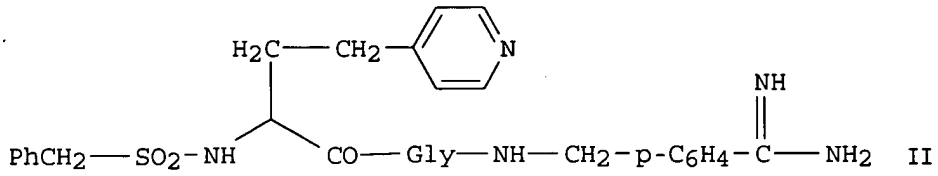


II

AB The invention relates to novel base-substituted benzylamine compds., e.g. (I), and their use as coagulation factor Xa inhibitors. The invention also relates to the production and use of said analogs in the therapy and prophylaxis of cardiovascular diseases and thromboembolic events. Thus, Boc-Gly-4-(acetyloxamidino)benzylamide was Boc-deprotected, coupled with Boc-DL-homoAla(4-Pyr)-OH, the coupled product BOC-deprotected, coupled with phenylmethylsulfonyl chloride, and the final intermediate N-deoxy-acetylated to give (II). In tests for selectivity of activity against Factor Xa vs. activity against thrombin, I had Ki Factor Xa of 0.0036 μM, against thrombin 100 μM, for a selectivity of 27778.

AN 2005:260091 CAPLUS
DN 142:317080

TI Synthesis and use of base-substituted benzylamine analogs for use as coagulation factor Xa inhibitors in the treatment and prophylaxis of cardiovascular diseases and thromboembolic events

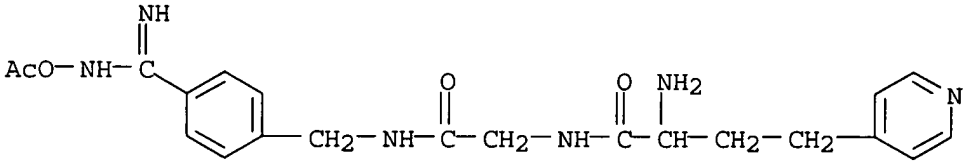
IN Sturzebecher, Jorg; Steinmetzer, Torsten; Schweinitz, Andrea; Sturzebecher, Anne; Donnecke, Daniel
PA Curacyte Chemistry GmbH, Germany

SO PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

4/28/05

PI WO 2005026198 A1 20050324 WO 2004-EP10225 20040913
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 10342108 A1 20050414 DE 2003-10342108 20030911
PRAI DE 2003-10342108 A 20030911
IT **848309-25-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and use of base-substituted benzylamine analogs for use as coagulation factor Xa inhibitors in the treatment and prophylaxis of cardiovascular diseases and thromboembolic events)
RN 848309-25-1 CAPLUS
CN 4-Pyridinebutanamide, N-[2-[[[4-[[(acetyloxy)amino]iminomethyl]phenyl]methyl]amino]-2-oxoethyl]-α-amino-, monohydrochloride (9CI) (CA INDEX NAME)

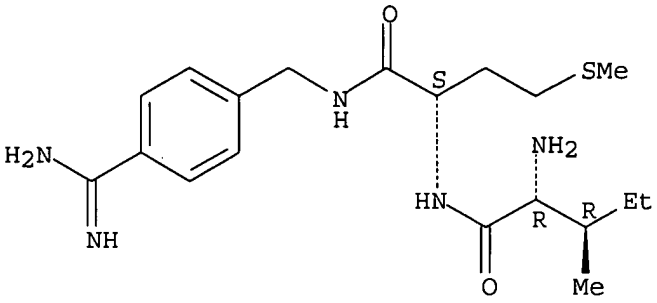



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
AB The 3D structure of human factor VIIa/soluble tissue factor in complex with a peptide mimetic inhibitor, propylsulfonamide-D-Thr-Met-p-aminobenzamidine, is determined by x-ray crystallog. As compared with the interactions between thrombin and thrombin inhibitors, the interactions at S2 and S3 sites characteristic of factor VIIa and factor VIIa inhibitors are revealed. The S2 site has a small pocket, which is filled by the hydrophobic methionine side chain in P2. The small S3 site fits the small size residue, D-threonine in P3. The structural data and SAR data of the peptide mimetic inhibitor show that these interactions in the S2 and S3 sites play an important role for the improvement of selectivity vs. thrombin. The results will provide valuable information for the structure-based drug design of specific inhibitors for FVIIa/TF.
AN 2004:886606 CAPLUS
DN 142:48484
TI Crystal structure of human factor VIIa/tissue factor in complex with peptide mimetic inhibitor

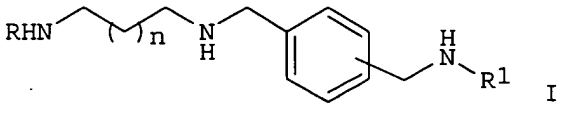
AU Kadono, Shojiro; Sakamoto, Akihisa; Kikuchi, Yasufumi; Oh-eda, Masayoshi; Yabuta, Naohiro; Koga, Takaki; Hattori, Kunihiro; Shiraishi, Takuya; Haramura, Masayuki; Kodama, Hirofumi; Esaki, Toru; Sato, Haruhiko; Watanabe, Yoshiaki; Itoh, Susumu; Ohta, Masateru; Kozono, Toshiro
CS Fuji Gotemba Research Labs, Chugai Pharmaceutical Co., Ltd., Gotemba, Shizuoka, 412-8513, Japan
SO Biochemical and Biophysical Research Communications (2004), 324(4), 1227-1233
CODEN: BBRCA9; ISSN: 0006-291X
PB Elsevier
DT Journal
LA English
IT **446845-92-7**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(crystal structure of human factor VIIa/tissue factor in complex with peptide mimetic inhibitor in relation to selectivity vs. thrombin)
RN 446845-92-7 CAPLUS
CN L-Methioninamide, L-isoleucyl-N-[[4-(aminoiminomethyl)phenyl]methyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.




RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
GI

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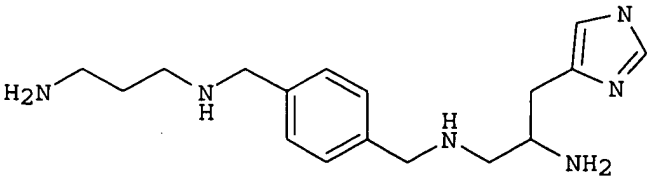



II

AB Novel polyamines, their synthesis and use in pharmacol., cosmetic or agricultural applications are provided. Novel polyamines having the structure (I) [wherein, n = 0-8; the aminomethyl functionality can be ortho, meta or para substituted; R = H, Me, Et, 2-aminoethyl, 3-aminopropyl, 4-aminobutyl, 5-aminopentyl, 6-aminohexyl, 7-aminoheptyl, 8-aminooctyl, N-methyl-2-aminoethyl, N-methyl-3-aminopropyl, N-methyl-4-aminobutyl, N-methyl-5-aminopentanyl, N-methyl-6-aminohexyl, N-methyl-7-aminoheptyl, N-methyl-8-aminooctyl, N-ethyl-2-aminoethyl, N-ethyl-3-aminopropyl, N-ethyl-4-aminobutyl, N-ethyl-5-aminopentyl, N-ethyl-6-aminohexyl, N-ethyl-7-aminoheptyl, N-ethyl-8-aminooctyl; R1 = H, straight or branched C1-20 (un)saturated aliphatic, aliphatic amine (except for propylamine when R = H, n=1 and the aminomethyl functionality is para substituted), alicyclic group, single or multi-ring aromatic group, single or multi-ring aryl substituted aliphatic group, aliphatic-substituted single or multi-ring aromatic group, single or multi-ring heterocyclyl, single or multi-ring heterocyclic-substituted aliphatic, aliphatic-substituted aromatic group, halogenated forms thereof; wherein said polyamine is a non-sym. xylene] are prepared Also provided are the use of the polyamines in pharmacol., cosmetic or agricultural applications. The polyamines induce antizyme production which in turn down regulates both the production of polyamines by ornithine decarboxylase (ODC) and the transport of polyamines by its corresponding polyamine transporter. These compds. will preferably enter the cell independent of the polyamine transporter. As drugs, these compds. are used as fungal, bacterial, viral and parasitic agents or to treat any disease associated with cellular proliferation including cancer, mucositis, asthma, inflammation, autoimmune disease, psoriasis, restentosis, rheumatoid arthritis, scleroderma, systemic and cutaneous lupus erythematosus, Type I insulin dependent diabetes, tissue transplantation, osteoporosis, hyperparathyroidism, treatment of peptic ulcer, glaucoma, Alzheimer's disease, Crohn's disease, and other inflammatory bowel diseases. A series of compds. I were screened for their ability to induce frameshifting using the dual luciferase reporter assay in HEK-293 cells. Some of these compds. induced frameshifting substantially better than spermidine. For example, compound (II) showed the percent relative frameshifting value (% RF) of 150% compared to 25 μM spermidine.

AN 2004:878166 CAPLUS
DN 141:366226
TI Preparation of polyamine analogs that activate antizyme frameshifting
IN Burns, Mark R.; Graminski, Gerard F.
PA Mediquest Therapeutics, Inc., USA
SO U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part of U.S. Ser. No. 251,819. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

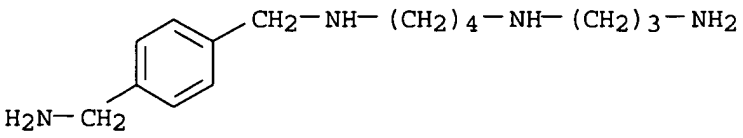
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004209926 | A1 | 20041021 | US 2004-810649 | 20040329 |
| | US 2004058954 | A1 | 20040325 | US 2002-251819 | 20020923 |
| PRAI | US 2002-251819 | A2 | 20020923 | | |

OS MARPAT 141:366226
IT **673461-33-1P**, 1-Aminomethyl-4-(10-amino-2,7-diazadecyl)benzene
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polyamine analogs as activating agents for antizyme

frameshifting to treat diseases associated with cellular proliferation or as antifungal, antibacterial, antiviral and antiparasitic agents)

RN 673461-33-1 CAPLUS

CN 1,4-Benzenedimethanamine, N-[4-[(3-aminopropyl)amino]butyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

AB A covalently reactive ligand analog (CAL) of formula [L1...Lx(L'-Y"-Y'-Y)...Lm]n: wherein, L1...Lx...Lm are components defining a ligand determinant, LX is a component unit of the ligand determinant selected from the group consisting of an amino acid residue, sugar residue, a fatty acid residue and a nucleotide, L' is a functional group of LX, Y' is atom, covalent bond or linker, Y' is an optional charged or neutral group Y is a covalently reactive electrophilic group that reacts specifically with a receptor that binds to said ligand determinant, and n is an integer from 1 to 1000 m is an integer from 1 to 30.

AN 2004:857331 CAPLUS

DN 141:346124

TI Covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy, immunoassays and purification of recombinant proteins

IN Paul, Sudhir; Nishiyama, Yasuhiro

PA The University of Texas, USA

SO PCT Int. Appl., 144 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004087059 | A2 | 20041014 | WO 2004-US9399 | 20040326 |

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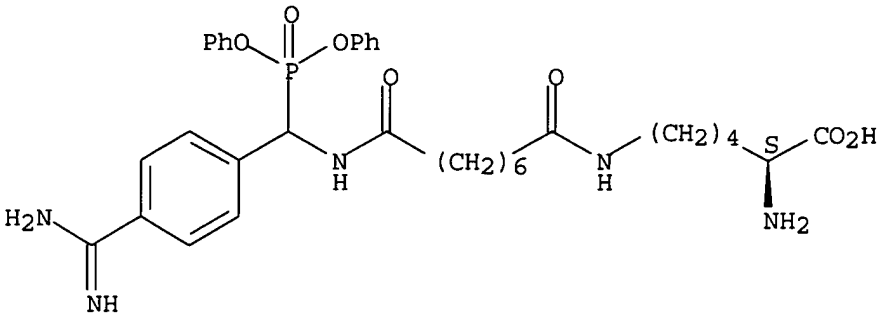
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-457293P P 20030326

IT **775343-00-5DP**, conjugates
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(L'-Y"-Y'-Y segment; covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

RN 775343-00-5 CAPLUS
CN L-Lysine, N6-[8-[[[4-(aminoiminomethyl)phenyl](diphenoxyphosphinyl)methyl]amino]-1,8-dioxooctyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
AB The invention provides biol. active compds. that may be reacted with macromols., e.g. albumin, to form covalently linked complexes, wherein the resulting complexes exhibit a desired biol. activity in vivo. More specifically, the complexes are isolated complexes comprising a biol. active moiety covalently bound to a linking group and a protein. The complexes are prepared by conjugating a biol. active moiety, e.g. a renin inhibitor or a viral fusion inhibitor peptide, with purified and isolated protein. The complexes have extended lifetimes in the bloodstream as compared to the unconjugated mol., and exhibit biol. activity for extended periods of time as compared to the unconjugated mol. The invention also provides antiviral compds. that are inhibitors of viral infection and/or exhibit anti-fusiogenic properties. In particular, the invention provides compds. having inhibiting activity against viruses such as human immunodeficiency virus (HIV), respiratory syncytial virus (RSV), human parainfluenza virus (HPV), measles virus (MeV), and simian immunodeficiency virus (SIV) and that have extended duration of action for the treatment of viral infections.
AN 2004:823936 CAPLUS
DN 141:325786
TI Long-acting conjugates of biologically active compounds with macromolecules, and their therapeutic use
IN Silva, Abelardo; Erickson, John E.; Eissenstat, Michael; Afonina, Elena; Gulnik, Sergei
PA Sequoia Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2004085505 | A2 | 20041007 | WO 2004-US8847 | 20040324 |

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TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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PRAI US 2003-456472P P 20030324
US 2003-456952P P 20030325
US 2003-518892P P 20031110

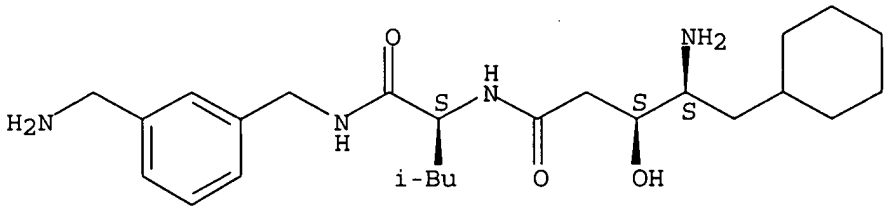
OS MARPAT 141:325786

IT **769922-28-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long-acting conjugates of biol. active compds. with macromols., and therapeutic use)

RN 769922-28-3 CAPLUS

CN L-threo-Pentonamide, 4-amino-N-[(1S)-1-[[[[3-(aminomethyl)phenyl]methyl]amino]carbonyl]-3-methylbutyl]-2,4,5-trideoxy-5-cyclohexyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



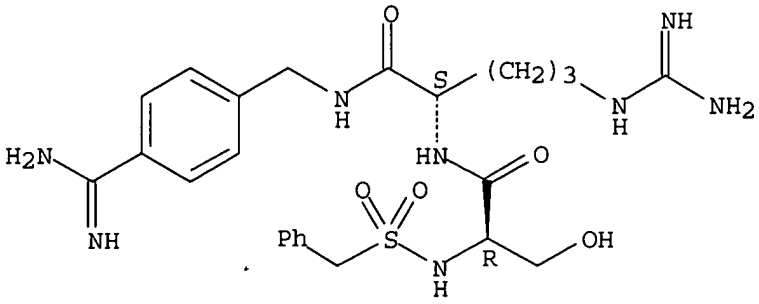

L4 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

AB The serine protease urokinase-type plasminogen activator (uPA) interacts with a specific receptor (uPAR) on the surface of various cell types, including tumor cells, and plays a crucial role in pericellular proteolysis. High levels of uPA and uPAR often correlate with poor prognosis of cancer patients. Therefore, the specific inhibition of uPA with small mol. active-site inhibitors is one strategy to decrease the invasive and metastatic activity of tumor cells. The authors have developed a series of highly potent and selective uPA inhibitors with a C-terminal 4-amidinobenzylamide residue. Optimization was directed toward reducing the fast elimination from circulation that was observed with initial analogs. The x-ray structures of three inhibitor/uPA complexes have been solved and were used to improve the inhibition efficacy. One of the most potent and selective derivs., benzylsulfonyl-D-Ser-Ser-4-amidinobenzylamide (inhibitor 26), inhibits uPA with a Ki of 20 nM. This inhibitor was used in a fibrosarcoma model in nude mice using lacZ-tagged human HT1080 cells, to prevent exptl. lung metastasis formation. Compared with control (100%), an inhibitor dose of 2 + 1.5 mg/kg/day reduced the number of exptl. metastases to 4.6±1%. Under these conditions inhibitor 26 also significantly prolonged survival. All mice from the control group died within 43 days after tumor cell inoculation, whereas 50% of mice from the inhibitor-treated group survived more than 117 days. This study demonstrates that the specific inhibition of uPA by these inhibitors may be a useful strategy for the treatment of cancer to prevent metastasis.

AN 2004:617178 CAPLUS

DN 141:270994
TI Design of Novel and Selective Inhibitors of Urokinase-type Plasminogen Activator with Improved Pharmacokinetic Properties for Use as Antimetastatic Agents
AU Schweinitz, Andrea; Steinmetzer, Torsten; Banke, Ingo J.; Arlt, Matthias J. E.; Stuerzebecher, Anne; Schuster, Oliver; Geissler, Andreas; Giersiefen, Helmut; Zeslawska, Ewa; Jacob, Uwe; Krueger, Achim; Stuerzebecher, Joerg
CS Curacyte Chemistry GmbH, Jena, D-07745, Germany
SO Journal of Biological Chemistry (2004), 279(32), 33613-33622
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
IT **600142-25-4DP**, and complex with urokinase-type plasminogen activator
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design of novel and selective inhibitors of urokinase-type plasminogen activator with improved pharmacokinetic properties for use as antimetastatic agents)
RN 600142-25-4 CAPLUS
CN L-Argininamide, N-[(phenylmethyl)sulfonyl]-D-seryl-N-[[4-(aminoiminomethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
AB The invention discloses the use of acylated 4-amidino or 4-guanidinobenzylamines P4-P3-P2-P1 [P4 = single or multiple (un)substituted benzylsulfonyl; P3 = single or multiple (un)substituted, (un)natural α-amino or α-imino acid in D-configuration; P2 = single or multiple (un)substituted, (un)natural α-amino or α-imino acid in L-configuration; P1 = single or multiple (un)substituted 4-amidino or 4-guanidinobenzylamine] for inhibition of plasma kallikrein (PK). The PK inhibitors of the invention are used for prevention of coagulation activation on artificial surfaces and for systemic addition as anticoagulants/antithrombotics, particularly for prevention of the coagulation activation on artificial surfaces, in order to prevent thromboembolic events. Compound preparation is included.
AN 2004:605410 CAPLUS

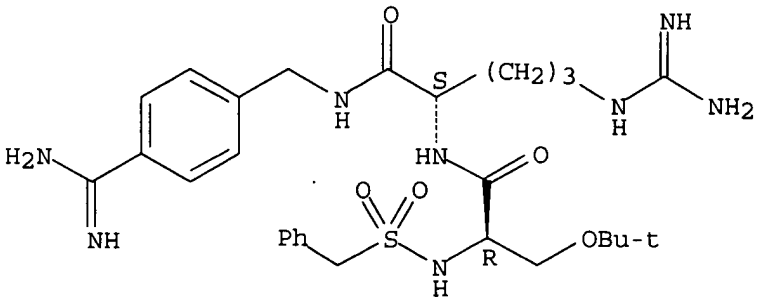
DN 141:150999
TI Use of acylated 4-amidino- and 4-guanidinobenzylamines for inhibition of plasma kallikrein
IN Sturzebecher, Jorg; Steinmetzer, Torsten; Schweinitz, Andrea
PA Curacyte Chemistry GmbH, Germany
SO Ger. Offen., 40 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10301300 | A1 | 20040729 | DE 2003-10301300 | 20030115 |
| WO 2004062657 | A1 | 20040729 | WO 2004-EP247 | 20040115 |
| WO 2004062657 | C1 | 20050106 | | |

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ

PRAI DE 2003-10301300 A 20030115
IT **600142-13-0**
RL: DEV (Device component use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acylated 4-amidino- and 4-guanidinobenzylamines for inhibition of plasma kallikrein)
RN 600142-13-0 CAPLUS
CN L-Argininamide, O-(1,1-dimethylethyl)-N-[(phenylmethyl)sulfonyl]-D-seryl-N-[[4-(aminoiminomethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



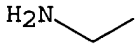

L4 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
AB A CXCR4 antagonistic peptide, T140, and its analogs, such as Ac-TE14011, inhibit the entry of T cell line-tropic strains of HIV-1 (X4-HIV-1) into T cells. Herein, a series of TE14011 analogs having modifications with Nα-acylation by several benzoic acid derivs. in the N-terminal region were synthesized to develop effective compds. with increased biostability. Among these analogs, 4F-benzoyl-TE14011 showed the strongest anti-HIV activity due to CXCR4-antagonism. Structure-activity relation (SAR) studies on TE14011 analogs have disclosed a significant relation between the anti-HIV activity and the Hammett constant (σ) of

substituted benzoic acids, suggesting that a 4-fluorobenzoyl moiety at the N-terminus of T140 analogs constitutes a novel T140-based pharmacophore for CXCR4 antagonism. Furthermore, identification of a T140-based new pharmacophore led to development of novel low-mol.-weight CXCR4 antagonists.

AN 2004:314191 CAPLUS
DN 141:235645
TI New leads of low molecular weight CXCR4 antagonists based on enhancement of the T140-based pharmacophores
AU Mizokami, Satoko; Tamamura, Hirokazu; Hiramatsu, Kenichi; Mizumoto, Makiko; Akamatsu, Miki; Nakashima, Hideki; Wang, Zixuan; Peiper, Stephen C.; Yamamoto, Naoki; Otaka, Akira; Fujii, Nobutaka
CS Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SO Peptide Science (2003), Volume Date 2004, 40th, 285-288
CODEN: PSCIFQ; ISSN: 1344-7661
PB Japanese Peptide Society
DT Journal
LA English
IT **664334-43-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leads of low mol. weight CXCR4 antagonists based on enhancement of T140-based pharmacophores)
RN 664334-43-4 CAPLUS
CN L-Argininamide, N2-[4-(aminomethyl)benzoyl]-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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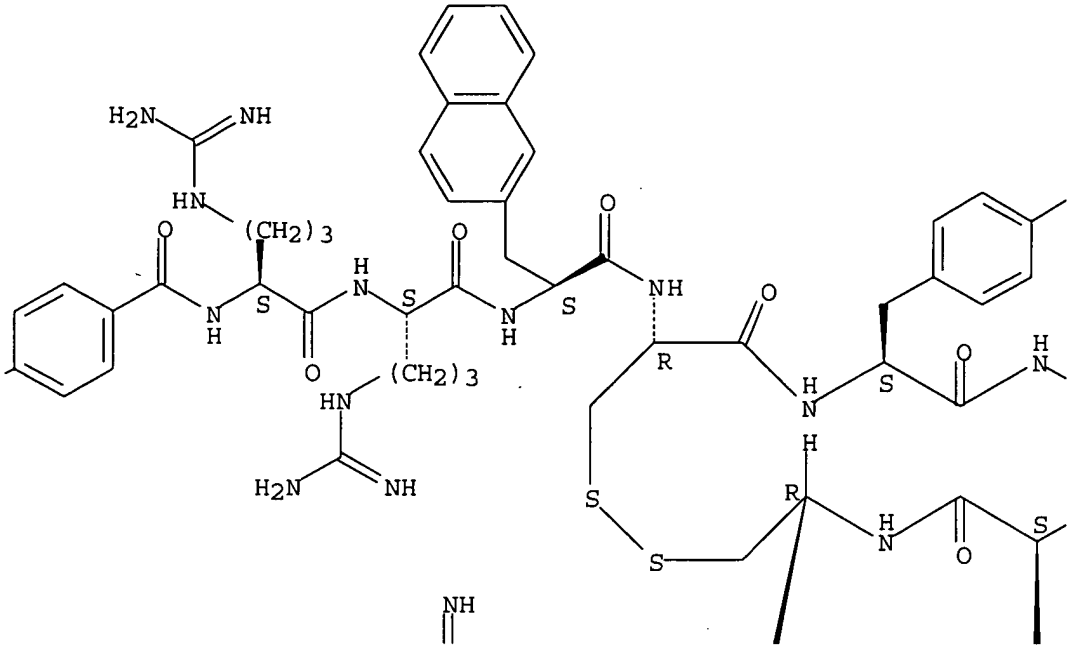

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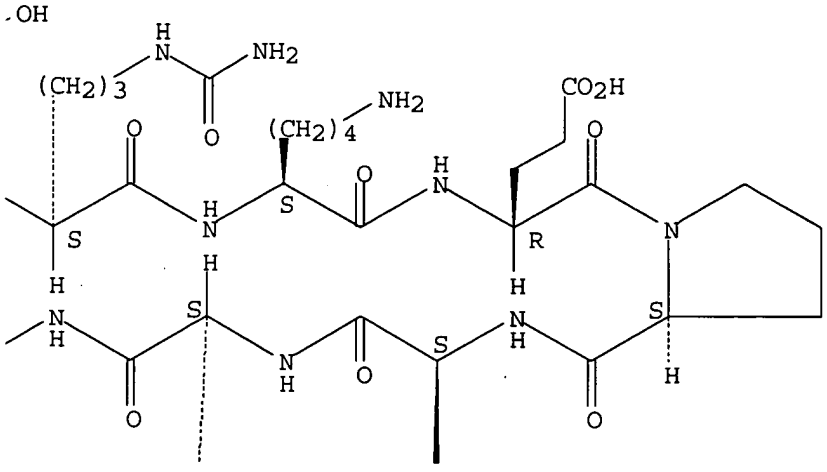
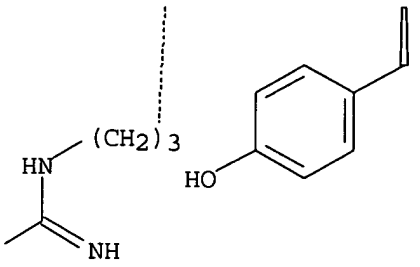


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *




RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

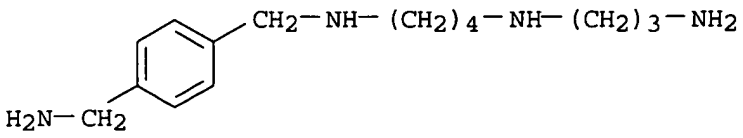
L4 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

AB The invention provides synthesis and use of polyamines in pharmacol., cosmetic or agricultural applications. The polyamines induce antizyme production which in turn down regulates both the production of polyamines by ornithine decarboxylase (ODC) and the transport of polyamines by its corresponding polyamine transporter. These compds. will preferably enter the cell independent of the polyamine transporter. As drugs, these compds. are used to treat any disease associated with cellular proliferation including but not limited to cancer. As such, they will be useful as drugs to treat diseases where components of the immune system undergo undesired proliferation. The compds. will also be effective for the treatment of unwanted proliferation of hair or skin. The invention also identifies key structural elements expected to comprise the antizyme inducing motifs of small mols. related to polyamines.

AN 2004:252193 CAPLUS
DN 140:264534
TI Polyamine analogs that activate antizyme framshifting
IN Burns, Mark R.; Graminski, Gerard F.
PA Mediquest Therapeutics, Inc., USA
SO U.S. Pat. Appl. Publ., 29 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004058954 | A1 | 20040325 | US 2002-251819 | 20020923 |
| | US 2004209926 | A1 | 20041021 | US 2004-810649 | 20040329 |
| PRAI | US 2002-251819 | A2 | 20020923 | | |

OS MARPAT 140:264534
IT **673461-33-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polyamine analogs that activate antizyme framshifting)
RN 673461-33-1 CAPLUS
CN 1,4-Benzenedimethanamine, N-[4-[(3-aminopropyl)amino]butyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

AB A CXCR4 antagonistic peptide, T140, and its bio-stable analogs, such as Ac-TE14011, were previously developed. These peptides inhibit the entry of T cell line-tropic strains of HIV-1 (X4-HIV-1) into T cells. Herein, a series of TE14011 analogs having modifications in the N-terminal region were synthesized to develop effective compds. with increased biostability. Among these analogs, 4F-benzoyl-TE14011 (TF14013) showed the strongest anti-HIV activity derived from CXCR4-antagonism, suggesting that a 4-fluorobenzoyl moiety at the N-terminus of T140 analogs constitutes a novel T140-based pharmacophore for CXCR4 antagonists. Structure-activity relationship (SAR) studies on TE14011 analogs with Nα-acylation by several benzoic acid derivs. have disclosed a significant relationship between the anti-HIV activity and the Hammett constant (σ) of substituted benzoic acids. TF14013 was found to be stable in mouse serum, but not completely stable in rat liver homogenate due to deletion of the C-terminal Arg14-NH2 from the parent peptide. This biodegrdn. was completely suppressed by N-alkyl-amidation at the C-terminus. Taken together, the enhancement of the T140-based pharmacophores led to development of a novel CXCR4 antagonist, 4F-benzoyl-TE14011-Me (TF14013-Me), which has very high anti-HIV activity and increased biostability.

AN 2003:833174 CAPLUS
DN 140:209914

TI Enhancement of the T140-based pharmacophores leads to the development of more potent and bio-stable CXCR4 antagonists

AU Tamamura, Hirokazu; Hiramatsu, Kenichi; Mizumoto, Makiko; Ueda, Satoshi; Kusano, Shuichi; Terakubo, Shigemi; Akamatsu, Miki; Yamamoto, Naoki; Trent, John O.; Wang, Zixuan; Peiper, Stephen C.; Nakashima, Hideki; Otaka, Akira; Fujii, Nobutaka

CS Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan

SO Organic & Biomolecular Chemistry (2003), 1(21), 3663-3669
CODEN: OBCRAK; ISSN: 1477-0520

PB Royal Society of Chemistry

DT Journal

LA English

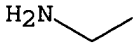
IT **664334-43-4P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(development of more potent and bio-stable CXCR4 antagonists by enhancement of T140-based pharmacophores)

RN 664334-43-4 CAPLUS

CN L-Argininamide, N2-[4-(aminomethyl)benzoyl]-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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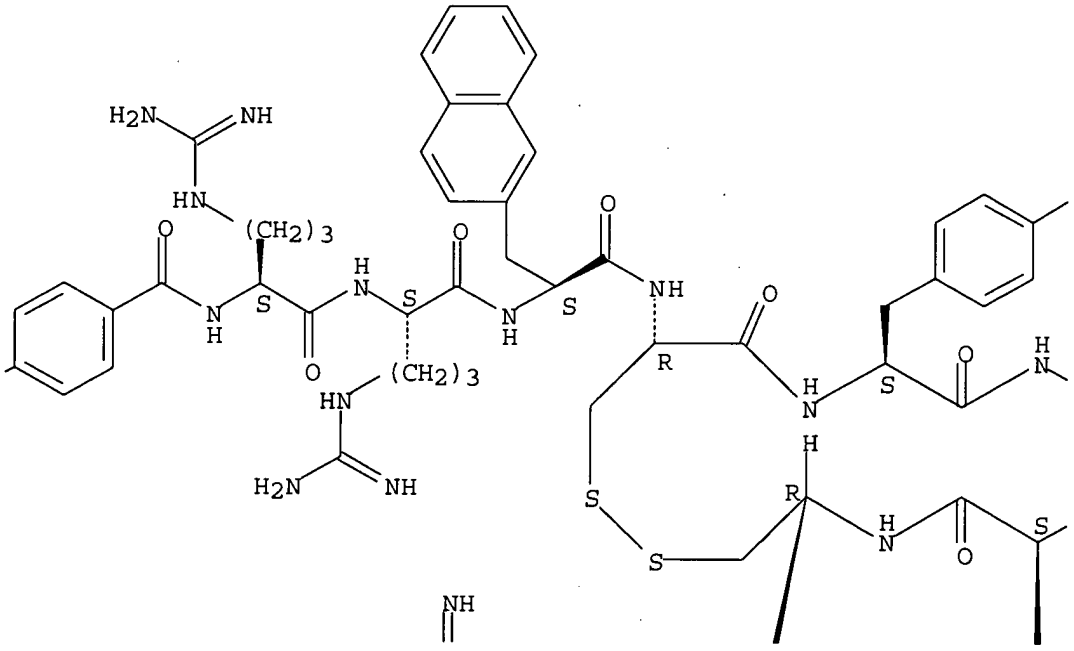

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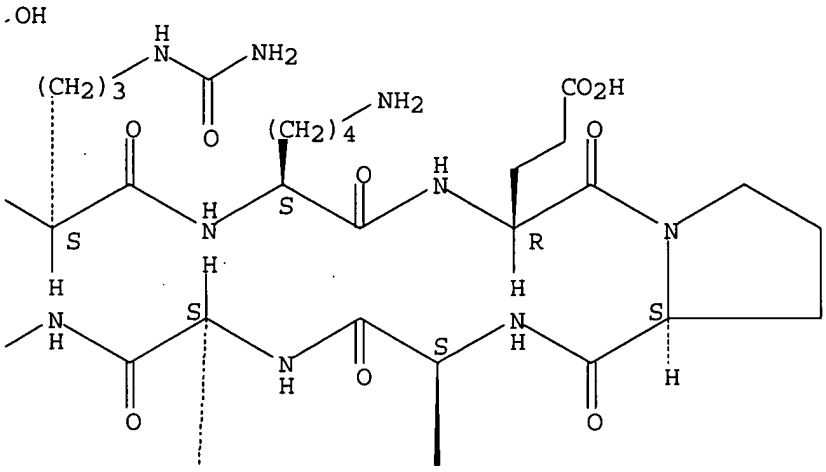
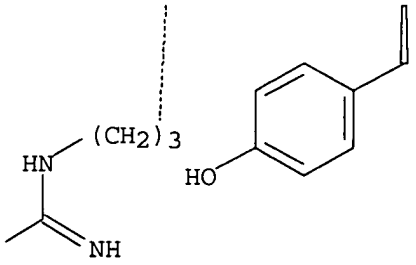


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

AB Title compds., [e.g., PhCH2SO2-D-Ser-Ser-NHCH2-4-C6H4-C(:NH)NH2 (I)], were prepared and tested as urokinase inhibitors, for use in the prophylaxis and diagnosis of a tumor and for reducing the formation of tumor metastases. Thus, (H3C)3COC(O)-Ser(CH2PH)-OH was reacted with H2NCH2-4-C6H4-C(:NH)NH2.HCl, the amine protecting group removed, and the intermediate reacted with PhCH2SO2-D-Ser(C(CH3)3)-OH; the intermediate protected dipeptide was purified by isolation as first the acetate salt, then the trifluoracetate salt, in a final yield of 24.64%. In in vivo tests against fibrosarcoma using white mice, after 22 days I reduced metastatic lung tumors by 4.6%, compared with a control group.

AN 2003:737714 CAPLUS

DN 139:246220
TI Synthesis of guanidinylbenzene-derivative dipeptide conjugate urokinase inhibitors as pharmaceuticals for use in the treatment or diagnosis of metastatic tumors
IN Sturzebecher, Jorg; Steinmetzer, Torsten; Schweinitz, Andrea
PA Curacyte Ag, Germany
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003076391 | A2 | 20030918 | WO 2003-EP2489 | 20030311 |
| | WO 2003076391 | A3 | 20040122 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
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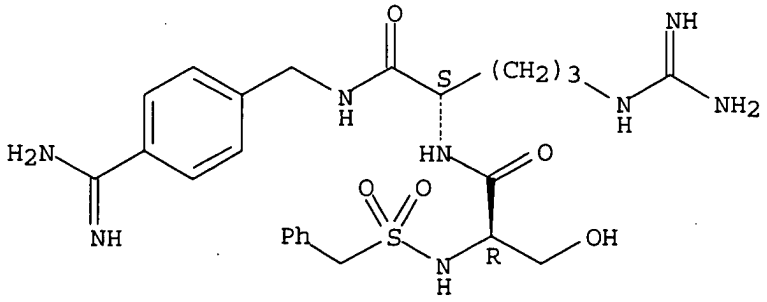
| | DE 10210592 | A1 | 20031002 | DE 2002-10210592 | 20020311 |
| | CA 2478409 | AA | 20030918 | CA 2003-2478409 | 20030311 |
| | EP 1485345 | A2 | 20041215 | EP 2003-714803 | 20030311 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

PRAI DE 2002-10210592 A 20020311
DE 2002-10245059 A 20020926
DE 2002-10261435 A 20021228
WO 2003-EP2489 W 20030311
OS MARPAT 139:246220
IT **600142-25-4**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of guanidinylbenzene-derivative dipeptide conjugate urokinase inhibitors as pharmaceuticals for use in the treatment or diagnosis of metastatic tumors)
RN 600142-25-4 CAPLUS
CN L-Argininamide, N-[(phenylmethyl)sulfonyl]-D-seryl-N-[[4-(aminoiminomethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

AB Claimed are CXCR4 antagonist drugs containing N-containing compds. A1(CH2)nWxCH[(CH2)mA2]yD (A1 and A2 represents each guanidino, A3B1NR1, etc.; A3 represents a monocyclic or polycyclic aromatic heterocycle having 1 or 2 hetero atoms; B1 represents a single bond or alkylene; and R1 represents hydrogen or alkyl; W represents C2-3 alkylene, C5-10 cycloalkylene, C6-10 aromatic cycle or C5-10 aromatic heterocycle; y is CO; x is CONH; n is an integer of 1 or 2; m is an integer of 2 or 3; and D is selected from among various substituents) or pharmacol. acceptable salts thereof as active ingredients. The bioactivities and toxicity of the title compds. were demonstrated. The title compds. are remedies for rheumatism, cancer metastasis, etc. Formulations are given.

AN 2002:905852 CAPLUS

DN 138:11404

TI CXCR4 antagonistic drugs comprising nitrogen-containing compounds

IN Yanaka, Mikiro; Yamazaki, Toru; Bannai, Kenji; Hirose, Kunitaka

PA Kureha Chemical Industry Co., Ltd., Japan

SO PCT Int. Appl., 227 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2002094261 | A1 | 20021128 | WO 2002-JP4846 | 20020520 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1389460 | A1 | 20040218 | EP 2002-771732 | 20020520 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | US 2004157818 | A1 | 20040812 | US 2004-478290 | 20040116 |
| PRAI | JP 2001-154904 | A | 20010524 | | |
| | WO 2002-JP4846 | W | 20020520 | | |

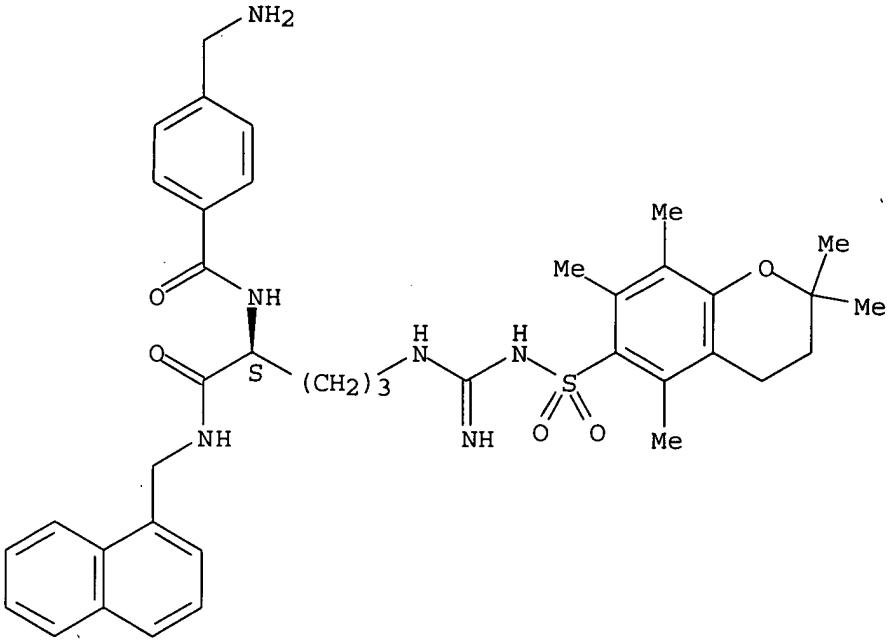
OS MARPAT 138:11404

IT **370594-84-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(CXCR4 antagonistic drugs comprising nitrogen-containing compds. and preparation of said compds.)

RN 370594-84-6 CAPLUS

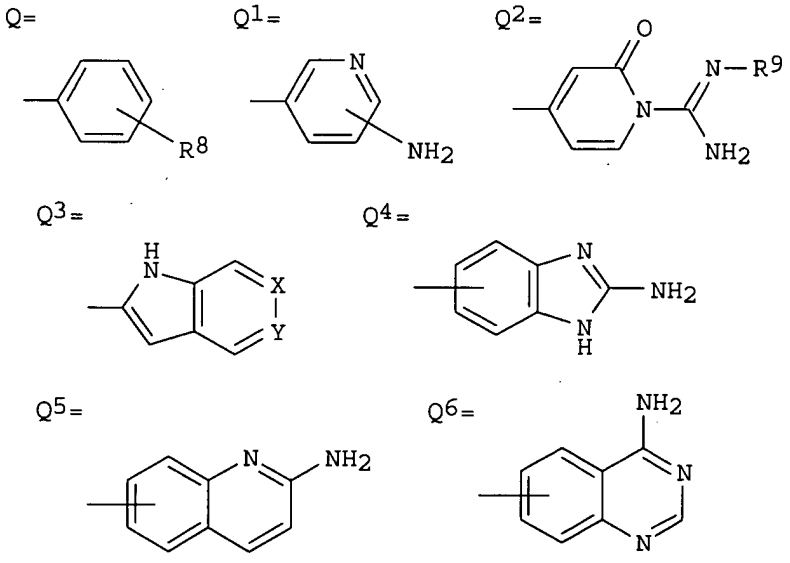
CN Benzamide, 4-(aminomethyl)-N-[(1S)-4-[[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]amino]-1-[[(1-naphthalenylmethyl)amino]carbonyl]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
GI



AB Dipeptide amide derivs. represented by the following general formula R1CH2NR2COCHR3NR4COCHR5NR6R7 [I; R1 = Q-Q6 (wherein R8 = NH2, aminomethyl, C(:NR9)NH2; R9 = H, NH2, OH, acyl, (un)substituted and linear or branched C1-6 alkoxy-carbonyl; one of X and Y is :CH and the other is N); R2 = H, linear or branched C1-6 alkyl; R3 = hydroxyphenyl, (CH2)mR11 (wherein R11

= CONH2, NR12CONH2, C(:NH)NH2; R12 = H, linear or branched C1-3 alkyl); R4 = H, linear or branched C1-6 alkyl; R7 = H, linear or branched C1-6 alkyl, SO2R14 (wherein R14 = linear or branched C1-8 alkyl)] are prepared Crystals of a complex of VIIa factor/human soluble tissue factor with a low-mol. weight reversible VIIa factor inhibitor selected from the dipeptide amide derivs. I are prepared and studied by X-ray crystal structure anal. Also disclosed is a medium carrying the whole or a part of the coordinate data of the stereostructure of the complex of human VIIa factor/human soluble tissue factor with a low-mol. weight reversible VIIa factor inhibitor obtained by X-ray crystal structure anal. of the above crystals recorded thereon. A method of designing a low-mol. weight reversible VIIa factor inhibitor by using the above data is claimed. These peptide derivs. are useful as antithrombotics for preventing or treating deep venous thrombosis after surgery, restenosis after PTCA surgery, chronic thrombosis such as chronic DIC, cardiac thromboembolism, or myocardial or cerebral infarction. Thus, 1-(tert-butoxycarbonyl)-D-tryptophyl-N1-(4-cyanobenzyl)-L-glutamine (preparation given) was condensed with 3-(methoxycarbonyl)benzylsulfonyl chloride in the presence of Et3N in DMF at room temperature for 12 h to give N-[[3-(methoxycarbonyl)benzyl]sulfonyl]-1-(tert-butoxycarbonyl)-D-tryptophyl-N1-(4-cyanobenzyl)-L-glutamine which was treated with saturated HCl/MeOH at room temperature for 20 h and refluxed with ammonium acetate and NH3 in ethanol for 1 h to give a mixture of N-[[3-(methoxycarbonyl)benzyl]sulfonyl]-D-tryptophyl-N1-(4-amidinobenzyl)-L-glutamine and N-[[3-(ethoxycarbonyl)benzyl]sulfonyl]-D-tryptophyl-N1-(4-amidinobenzyl)-L-glutamine. The latter mixture was stirred with a mixture of ethanol and 2 N aqueous EtOH at room temperature for 1 h and acidified with 1 N aqueous HCl to give N-[(3-carboxybenzyl)sulfonyl]-D-tryptophyl-N1-(4-amidinobenzyl)-L-glutamine (II). II in vitro inhibited factor VIIa and thrombin with IC50 of 37 and 17,870 nM, resp. A complex of human factor VII/human soluble tissue factor with N-(carboxymethylsulfonyl)-D-tryptophyl-N1-(4-amidinobenzyl)-L-glutamine and that with N-(ethanesulfonyl)-p-phenyl-D-phenylalanyl-N1-(4-amidinobenzyl)-L-glutamine were prepared in a crystalline form and studied by X-ray crystal structure anal.

AN 2002:615652 CAPLUS
DN 137:169797
TI Preparation of peptide derivatives as factor VIIa inhibitors
IN Shiraishi, Takuya; Kadono, Shojiro; Haramura, Masayuki; Sato, Haruhiko; Kozono, Toshiro; Koga, Takaki; Sakamoto, Akihisa
PA Chugai Seiyaku Kabushiki Kaisha, Japan
SO PCT Int. Appl., 246 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2002062829 | A1 | 20020815 | WO 2002-JP883 | 20020204 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1364960 A1 20031126 EP 2002-711294 20020204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2004087511 A1 20040506 US 2003-470801 20030801

PRAI JP 2001-27474 A 20010202

WO 2002-JP883 W 20020204

OS MARPAT 137:169797

IT **446845-92-7P**

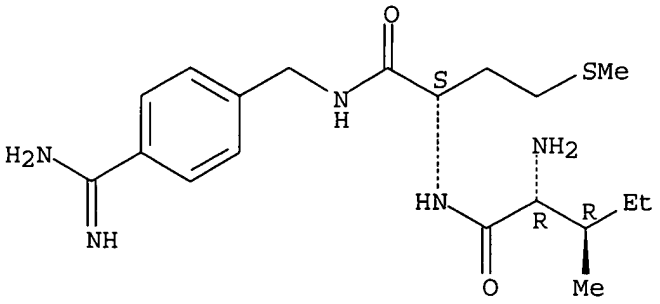
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptide derivs. as VIIa factor inhibitors and antithrombotics and X-ray crystal structure anal. of human VIIa factor-peptide inhibitor complex)

RN 446845-92-7 CAPLUS

CN L-Methioninamide, L-isoleucyl-N-[[4-(aminoiminomethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

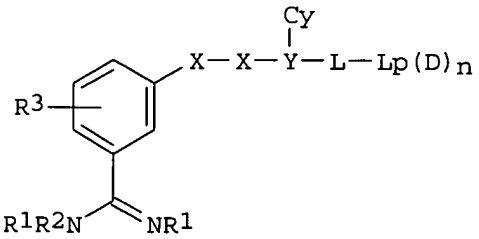
Absolute stereochemistry.




RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

GI




I

AB Title compds. I [R1, R2 = H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl, cycloalkyl; R3 = R1, R2, amino, halo, cyano, nitro, thiol, alkylthio,

alkylsulfonyl, alkylsulfenyl, alkylsulfonamido, alkylaminosulfonyl, haloalkoxy, haloalkyl; X = C, N, O, S, CO, CR1, C(R1)2, NR1 with at least one X being C, CO, CR1 or C(R1)2, with the proviso that if the benzamidine group is unsubstituted and the X-X group is -CH2C(R1)2-, then R1 = H or attached to the alkylene carbon atom by a heteroatom; L = organic linker containing 1-5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Y = N, CR1; YL = cyclic group; Cy = (un)saturated, (poly)cyclic, (hetero)cyclic group optionally substituted by groups R3 or Ph optionally substituted by R3; Lp = lipophilic alkyl, heterocyclic, alkenyl, alkaryl, (poly)cycloalkyl, cycloalkenyl, aryl, aralkyl, haloalkyl, or a combination of two or more such groups optionally substituted by oxa, oxo, aza, thio, halo, amino, hydroxy or by R3; D = H bond donor group; n = 0-2], or corresponding compds. in which the (un)substituted amidino group R1R2NC(:NR1) is replaced with an (un)substituted aminomethyl group, or their physiol. tolerable salts were prepared as serine protease inhibitors useful as antithrombotic agents. 3-Amidino- and 3-(aminomethyl)benzoyl-D-phenylglycine 4-aminomethylcyclohexylmethylamide are among 190 compds. synthesized.

AN 2002:354079 CAPLUS

DN 136:355487

TI Preparation of meta-benzamidine derivatives of amino acids or dipeptides as serine protease inhibitors

IN Liebeschuetz, John Walter; Wylie, William Alexander; Waszkowycz, Bohdan; Murray, Christopher William; Rimmer, Andrew David; Welsh, Pauline Mary; Jones, Stuart Donald; Roscoe, Jonathan Michael Ernest; Young, Stephen Clinton; Morgan, Phillip John

PA Tularik Ltd., UK

SO U.S. Pat. Appl. Publ., 35 pp., Cont.-in-part of U.S. Ser. No. 485,678. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 13

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2002055522 | A1 | 20020509 | US 2001-988082 | 20011119 |
| | US 6740682 | B2 | 20040525 | | |
| | WO 9911658 | A1 | 19990311 | WO 1998-GB2605 | 19980828 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | WO 2000077027 | A2 | 20001221 | WO 2000-GB2291 | 20000613 |
| | WO 2000077027 | A3 | 20010525 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
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| | US 2003216403 | A1 | 20031120 | US 2003-296245 | 20030514 |
| | US 2004143018 | A1 | 20040722 | US 2004-752568 | 20040108 |

PRAI GB 1997-18392 A 19970829
GB 1998-3173 A 19980213
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GB 1999-13823 A 19990614
US 1999-142064P P 19990702
US 2000-485678 A2 20000225
WO 2000-GB2291 A2 20000613
GB 1999-18741 A 19990809
GB 1999-29552 A 19991214
GB 1999-29553 A 19991214
WO 2001-GB2566 W 20010612
US 2001-988082 A1 20011119

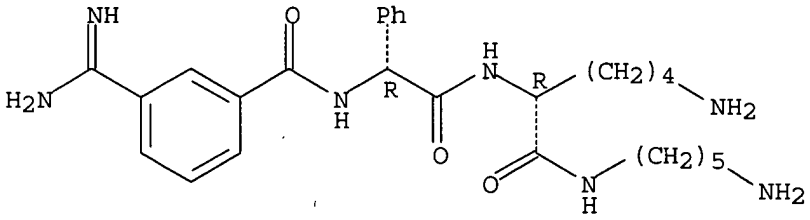
OS MARPAT 136:355487

IT **221232-83-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of meta-benzamidine derivs. of amino acids or dipeptides as serine protease inhibitors)

RN 221232-83-3 CAPLUS

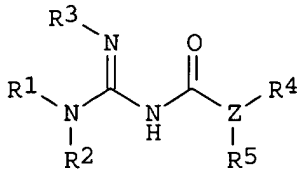
CN D-Lysinamide, (2R)-N-[3-(aminoiminomethyl)benzoyl]-2-phenylglycyl-N-(5-aminopentyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

GI



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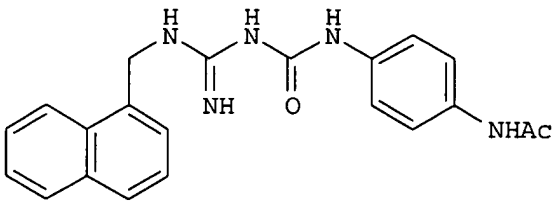


II

AB The title compds. [I; Z = N, O, CH; R1 = H, alkyl; R2 = (un)substituted alkyl, cycloalkyl, (hetero)arylalkyl; NR1R2 = (un)substituted 5-6 membered ring; R3 = H, alkyl, alkylaminocarbonyl; R4 = H, alkyl, alkenyl, etc.; R5 = absent (when Z = O), H, alkyl; ZR4R5 = (un)substituted 5-6 membered ring] which are novel 5-HT7 receptor ligands useful in treating sleep disorders, pain, depression, and schizophrenia, were prepared E.g., a 3-step synthesis of II which showed Ki of 13 nM at 5-HT7 receptor, was given.

AN 2002:353419 CAPLUS

DN 136:369519

TI Preparation of amidino-urea serotonin receptor ligands

IN Hong, Yufeng; Kuki, Atsuo; Tompkins, Eileen Valenzuela; Peng, Zhengwei; Luthin, David Robert

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2002036554 | A2 | 20020510 | WO 2001-IB2022 | 20011026 |
| | WO 2002036554 | A3 | 20030313 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2425285 | AA | 20020510 | CA 2001-2425285 | 20011026 |
| | AU 2001095836 | A5 | 20020515 | AU 2001-95836 | 20011026 |
| | EP 1332127 | A2 | 20030806 | EP 2001-976571 | 20011026 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | BR 2001015079 | A | 20030819 | BR 2001-15079 | 20011026 |
| | JP 2004522705 | T2 | 20040729 | JP 2002-539314 | 20011026 |
| | US 2004044037 | A1 | 20040304 | US 2003-415619 | 20030429 |
| PRAI | US 2000-243959P | P | 20001030 | | |
| | WO 2001-IB2022 | W | 20011026 | | |

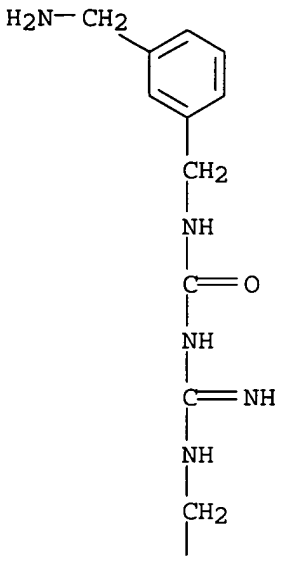
OS MARPAT 136:369519

IT **422567-68-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidino-urea serotonin receptor ligands)

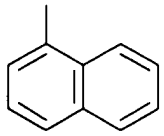
RN 422567-68-8 CAPLUS

CN Urea, N-[[3-(aminomethyl)phenyl]methyl]-N'-[imino[(1-naphthalenylmethyl)amino]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L4 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

AB A series of 4-amidinobenzylamine-based peptidomimetic inhibitors of urokinase was synthesized. The most potent one, benzylsulfonyl-d-Ser-Ala-4-amidinobenzylamide, inhibits uPA with a Ki of 7.7 nM but is less selective than 10 with a Gly as P2 residue. Hydroxyamidine and carbonate prodrugs were prepared, which are rapidly converted into the active inhibitors in rats after s.c. application.

AN 2002:116967 CAPLUS
DN 137:134463

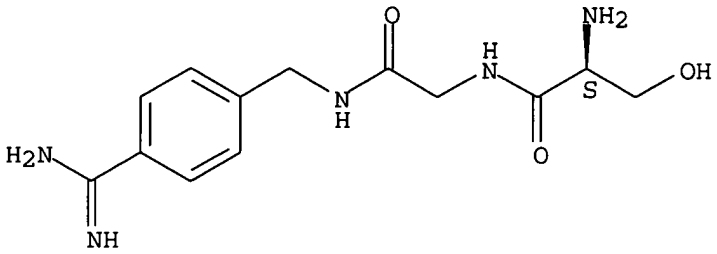
TI 4-Amidinobenzylamine-Based Inhibitors of Urokinase

AU Kunzel, Sebastian; Schweinitz, Andrea; Reissmann, Siegmund; Sturzebecher, Jorg; Steinmetzer, Torsten
CS Universitat Jena, Institut fur Biochemie und Biophysik, Jena, D-07743, Germany

SO Bioorganic & Medicinal Chemistry Letters (2002), 12(4), 645-648
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 137:134463

IT **380237-53-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure activity of amidinobenzylamine-based inhibitors of urokinase)
RN 380237-53-6 CAPLUS
CN Glycinamide, L-seryl-N-[[4-(aminoiminomethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



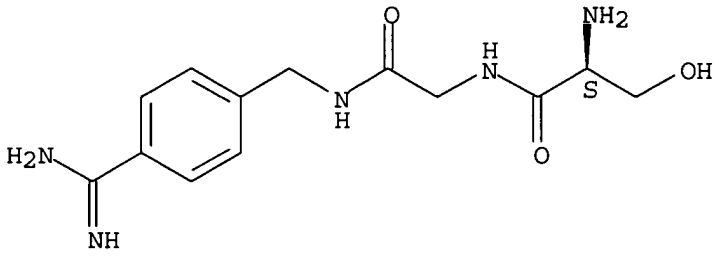
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
AB The invention provides derivs. of amidinobenzylamine, especially derivs. of 4-amidinobenzylamine, with two bonded amino acids. These derivs. represent a novel group of highly active and very selective FXa-inhibitors for treating cardiovascular diseases and thrombotic events.
AN 2001:923823 CAPLUS
DN 136:31691
TI Amidinobenzylamine derivatives as inhibitors for blood-clotting factor Xa, preparation, and therapeutic use
IN Sturzebecher, Jorg; Steinmetzer, Torsten; Kunzel, Sebastian; Schweinitz, Andrea
PA Curacyte A.-G., Germany
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

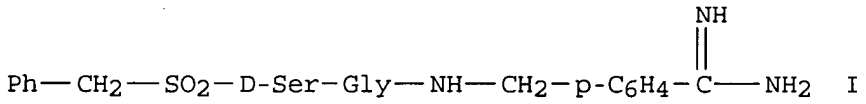
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001096366 | A2 | 20011220 | WO 2001-EP6814 | 20010615 |
| | W: AU, BR, CA, CR, JP, NO, NZ, US, ZA | | | | |
| | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| | DE 10029015 | A1 | 20011220 | DE 2000-10029015 | 20000615 |
| | CA 2412181 | AA | 20021209 | CA 2001-2412181 | 20010615 |
| | EP 1294741 | A2 | 20030326 | EP 2001-960319 | 20010615 |
| | EP 1294741 | B1 | 20050216 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | | |
| | JP 2004503563 | T2 | 20040205 | JP 2002-510507 | 20010615 |
| | AT 289319 | E | 20050315 | AT 2001-960319 | 20010615 |
| | US 2003166577 | A1 | 20030904 | US 2003-311364 | 20030321 |
| | US 6841701 | B2 | 20050111 | | |

PRAI DE 2000-10029015 A 20000615
WO 2001-EP6814 W 20010615
OS MARPAT 136:31691
IT **380237-53-6**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amidinobenzylamine derivs. as inhibitors for blood-clotting factor Xa, preparation, and therapeutic use)
RN 380237-53-6 CAPLUS
CN Glycinamide, L-seryl-N-[[4-(aminoiminomethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
GI



AB The invention relates to a highly active, highly specific urokinase inhibitor which is suitable for therapeutic applications or diagnosis of metastatic tumors, and can be synthesized in an extremely simple manner. It was found that amidino benzylamine derivs., especially 4-amidino-benzylamine, with two bonded amino acids [e.g., (I)] represent a new group of highly active and very selective uPA inhibitors. Beginning with 4-cyanobenzylamine, chloroformic acid iso-Bu ester, and H-D-Ser(CH2Ph)-OH, I was synthesized in 10 steps. I showed in vitro inhibition of urokinase activity with a Ki of 0.036 μM.
AN 2001:923749 CAPLUS
DN 136:37951
TI Preparation of D-Ser-Gly-amidinobenzylamide urokinase inhibitors for use in treatment of metastatic tumors.
IN Sturzebecher, Jorg; Steinmetzer, Torsten; Kunzel, Sebastian; Schweinitz, Andrea
PA Friedrich-Schiller- Universitat Jena, Germany
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA German

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001096286 | A2 | 20011220 | WO 2001-EP6789 | 20010615 |
| | WO 2001096286 | A3 | 20020627 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | DE 10029014 | A1 | 20011220 | DE 2000-10029014 | 20000615 |
| | CA 2411981 | AA | 20021209 | CA 2001-2411981 | 20010615 |
| | EP 1294742 | A2 | 20030326 | EP 2001-964989 | 20010615 |
| | EP 1294742 | B1 | 20040331 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | JP 2004503526 | T2 | 20040205 | JP 2002-510430 | 20010615 |
| | AT 263186 | E | 20040415 | AT 2001-964989 | 20010615 |
| | US 2003166576 | A1 | 20030904 | US 2002-297557 | 20021209 |
| | US 6831196 | B2 | 20041214 | | |
| PRAI | DE 2000-10029014 | A | 20000615 | | |
| | WO 2001-EP6789 | W | 20010615 | | |

OS MARPAT 136:37951

IT **380237-53-6**

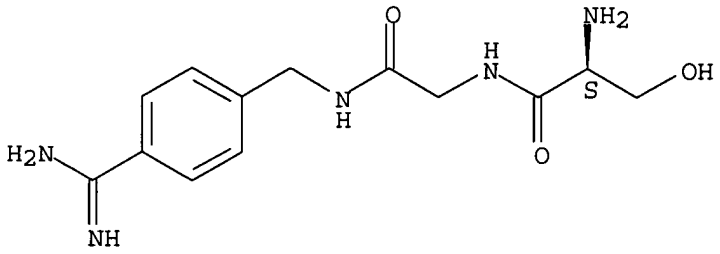
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of D-ser-gly-amidinobenzylamide urokinase inhibitors for use in treatment and diagnosis of metastatic tumors)

RN 380237-53-6 CAPLUS

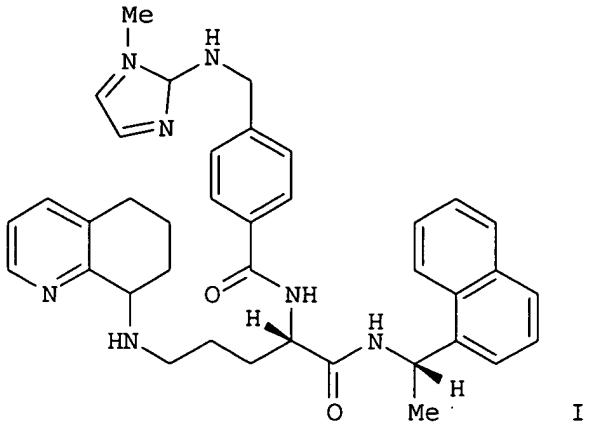
CN Glycinamide, L-seryl-N-[[4-(aminoiminomethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L4 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

GI



I

AB Novel nitrogenous compds. represented by general formula A1-(CH2)n1-W-X-CH[(CH2)n2-A2]-Y-D [n1 = 0-3; n2 = 0-4; A1, A2 = (un)substituted guanidino or amidino, A3-B1-NR1-, A3-CR2A4-NR1-; wherein A3, A4 = (un)substituted 5- to 12-membered mono- or polycyclic heterocyclyl which may be partially saturated; B1 = single bond, CR2R3; R1, R2, R3 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl or alkynyl, or R2 is bonded to R1 or R3 to form a ring; W = (un)substituted C1-7 alkylene, C2-7 alkenylene, C2-7 alkynylene, or group B [wherein group B = C3-10 mono- or polycyclic alkylene, (un)substituted 6- to 15-membered ring mono or polycyclic aryl which may be partially saturated, or (un)substituted 6- to 15-membered ring mono or polycyclic heterocyclyl optionally containing 1-3 of O, S, and N atoms and optionally partially saturated]; D = -W1-G1-G2-W2-G3; W1 = O, S, (un)substituted NR4 or NHNR4 (R4 = H, -G1'-G1'-G2'-W2'-G3'); G1, G1' = single bond, (un)substituted C1-10 alkylene or C2-10 alkenylene or alkynylene, etc.; G2, G2' = single bond, group B;W2, W2' = single bond, O, S, (un)substituted NH, etc.; G3, G3' = H, (un)substituted and linear or branched C1-6 alkyl, C2-6 alkenyl, group B, etc.; X = -Z1-Z-Z2-; wherein Z = CO, S, SO, SO2, (un)substituted CH2; Z1, Z2 = single bond, O, S, (un)substituted NH; Y = CO, S, SO, SO2] are prepared These compds. possess excellent antiretroviral activity and protective activity for cells infected with HIV-1 and are useful for the treatment of AIDS or AIDS-related complications. Thus, Nα-deprotection of Na-Fmoc-Nδ-Boc-L-ornithine (1S)-1-(1-naphthyl)ethylamide with diethylamine in DMF followed by condensation with 4-[N-Boc-N-(1-methylimidazol-2-yl)aminomethyl]benzoic acid using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and HOBt in DMF gave Nα-[4-[[(1-methylimidazol-2-yl)amino]methyl]benzoyl]-Nδ-Boc-L-ornithine N-[(1S)-1-(1-naphthyl)ethyl]amide which underwent Nδ-deprotection with a mixture of 4 M HCl/dioxane and methanol at room temperature for 2 h and reductive amination with 5,6,7,8-tetrahydroquinolin-8-one using sodium cyanoborohydride in methanol, followed by treatment with HCl to give (2S)-2-[[4-[[(1-methylimidazol-2-yl)amino]methyl]benzoyl]amino]-5-(5,6,7,8-tetrahydroquinolin-8-ylamino)valeric acid N-[(1S)-1-(1-naphthyl)ethyl]amide hydrochloride (I.xHCl). I.xHCl in vitro EC50 of 0.025 μM for inhibiting the cell injury of MT-4 cells infected with HIV-1IIIB. A tablet formulation containing Nα-[4-(N-2-picolylaminomethyl)-1-naphthylcarbonyl]-L-arginyl-D-3-(1-naphthyl)alanine was prepared

AN 2001:780851 CAPLUS
DN 135:344724

TI Preparation of amino acid amide and dipeptide derivatives and antiviral drugs containing the same

IN Yamazaki, Toru; Maruoka, Hiroshi; Suzuki, Shigeru; Mukade, Tsutomu; Hirose, Kunitaka; Yanaka, Mikiro; Yamamoto, Naoki

PA Kureha Chemical Industry Co., Ltd., Japan

SO PCT Int. Appl., 226 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001079168 | A1 | 20011025 | WO 2001-JP3123 | 20010411 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 2001048753 | A5 | 20011030 | AU 2001-48753 | 20010411 |
| | CA 2405690 | AA | 20021009 | CA 2001-2405690 | 20010411 |
| | EP 1273571 | A1 | 20030108 | EP 2001-921809 | 20010411 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | US 2004092556 | A1 | 20040513 | US 2002-257340 | 20021121 |
| PRAI | JP 2000-114067 | A | 20000414 | | |
| | WO 2001-JP3123 | W | 20010411 | | |

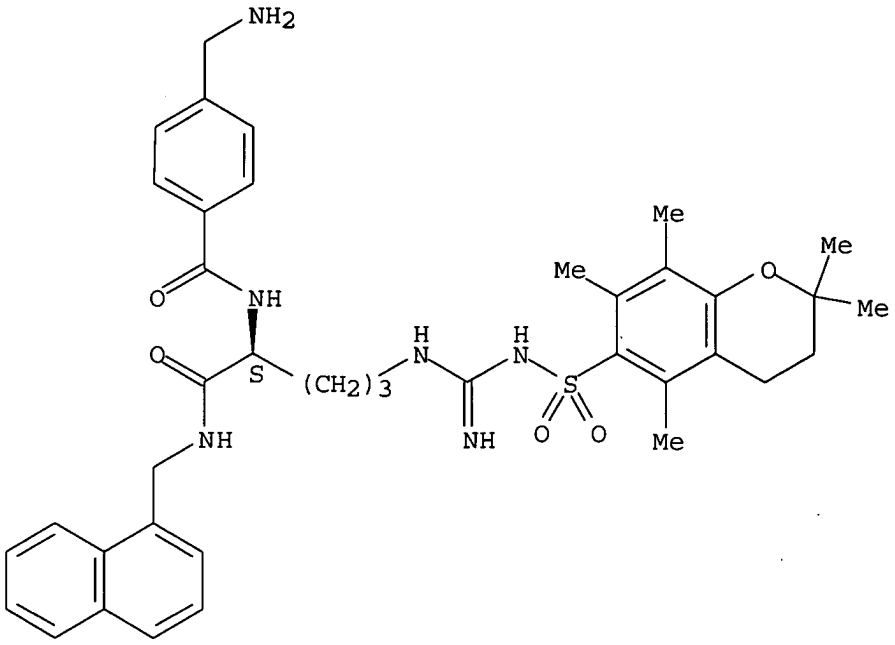
OS MARPAT 135:344724

IT **370594-84-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid amide and dipeptide derivs. as antiretroviral drugs for treatment of AIDS)

RN 370594-84-6 CAPLUS

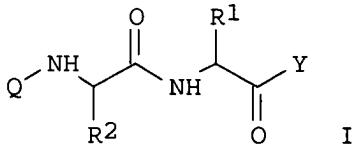
CN Benzamide, 4-(aminomethyl)-N-[(1S)-4-[[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]amino]-1-[[(1-naphthalenylmethyl)amino]carbonyl]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
GI



I

AB The present invention relates to compds. of general formula I wherein R1 represents a (C1-C7) alkyl group which can be substituted or a cycloalkyl or cycloalkylalkyl group or a (CH2)n-X-R3 group; R2 represents a (C1-C7) alkyl group which can be substituted or a cycloalkyl or cycloalkylalkyl group or a Ph, benzyl or 2-phenylethyl group which can be substituted on the Ph group or a carbocyclic or heterocyclic group; R3 is alkyl; n is 1-3; X is S, O; Y is represented by the two tautomeric forms of arylalkylamine; Q represents an R4-SO2- group wherein R4 represents a (C1-C8)alkyl group or a cycloalkylalkyl group or a benzyl group which can be substituted, were prepared as antithrombotic agents. Thus, (α,R)-N-[(1S)-1-[[[[4-(aminoiminomethyl)phenyl]methyl]amino]carbonyl ]pentyl]-α-[[(phenylmethyl)sulfonyl]amino]-1H-indole-3-propanamide hydrochloride was prepared and tested in rats for its antithrombotic activity.

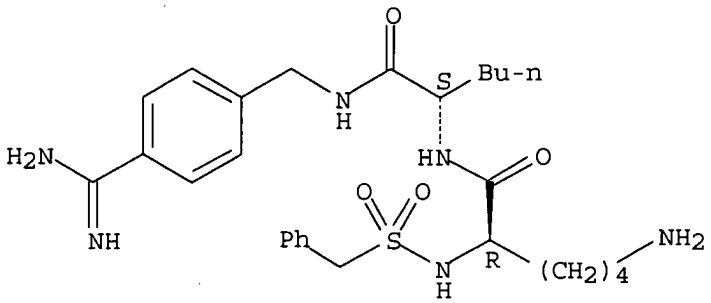
AN 2000:707197 CAPLUS
DN 133:267159
TI Preparation of N-sulfonyl-dipeptides as antithrombotic agents
IN Alcouffe, Chantal; Bellevergue, Patrice; Dellac, Genevieve; Latham, Christopher; Martin, Valerie; Masson, Christine; McCort, Gary

PA Sanofi-Synthelabo, Fr.
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000058346 | A1 | 20001005 | WO 2000-FR696 | 20000321 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| FR 2791683 | A1 | 20001006 | FR 1999-3933 | 19990330 |
| PRAI FR 1999-3933 | A | 19990330 | | |

OS MARPAT 133:267159
IT **296787-28-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-sulfonyl-dipeptides as antithrombotic agents)
RN 296787-28-5 CAPLUS
CN L-Norleucinamide, N2-[(phenylmethyl)sulfonyl]-D-lysyl-N-[[4-(aminoiminomethyl)phenyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




● HCl

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

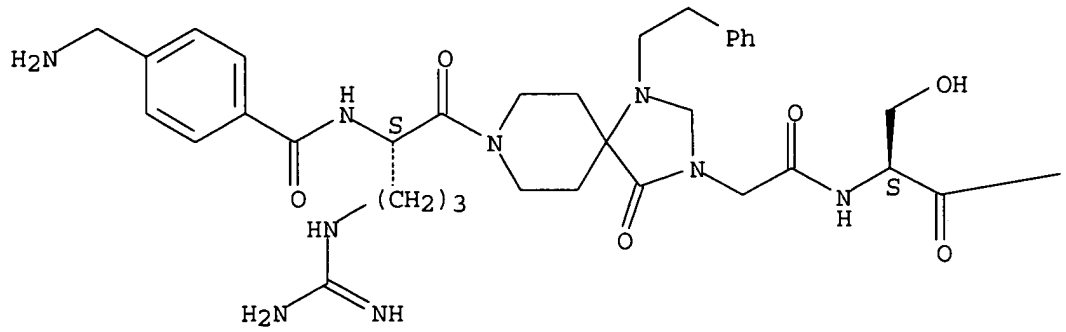
L4 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
AB We have previously synthesized a potent and selective B1 bradykinin receptor antagonist, JMV 1645 (H-Lys-Arg-Pro-Hyp-Gly-Igl-Ser-D-BT-OH), containing a dipeptide mimetic ((3S)-amino-5-carbonylmethyl-2,3-dihydro-1,5-benzothiazepin-4(5H)-one (D-BT) moiety) at the C-terminal. Analogs of

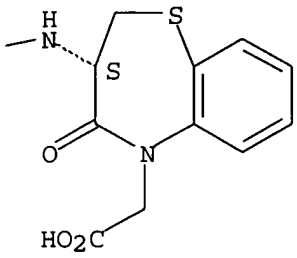
this potent B1 bradykinin receptor antagonist in which the central Pro2-Hyp3-Gly4-Igl5 tetrapeptide has been replaced by constrained N-1-substituted-1,3,8-triazaspiro[4.5]decan-4-one ring system were synthesized. Among these analogs, compound JMV 1640 was found to have an affinity of 24.10 ± 9.48 nM for the human cloned B1 receptor. It antagonized the [des-Arg10]-kallidin-induced contraction of the human umbilical vein (pA2 = 6.1 ± 0.1). Compound JMV 1640 was devoid of agonist activity at the kinin B1 receptor. Moreover, it did not bind to the human cloned B2 receptor. Therefore, JMV 1640 constitutes a lead compound for the rational search of nonpeptide B1 receptor analogs based on the BK sequence.

AN 2000:338366 CAPLUS
DN 133:177451
TI A Rational Approach to the Design and Synthesis of a New Bradykinin B1 Receptor Antagonist
AU Bedos, Philippe; Amblard, Muriel; Subra, Gilles; Dodey, Pierre; Luccarini, Jean-Michel; Paquet, Jean-Luc; Pruneau, Didier; Aumelas, Andre; Martinez, Jean
CS Laboratoire des Aminoacides Peptides et Proteines, Universites Montpellier I et II Faculte de Pharmacie, Montpellier, 34060, Fr.
SO Journal of Medicinal Chemistry (2000), 43(12), 2387-2394
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
IT **288154-12-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity relationship of Bradykinin B1 receptor antagonist)
RN 288154-12-1 CAPLUS
CN L-Serinamide, N2-[4-(aminomethyl)benzoyl]-L-arginyl-4-oxo-1-(2-phenylethyl)-1,3,8-triazaspiro[4.5]decane-3-acetyl-N-[(3S)-5-(carboxymethyl)-2,3,4,5-tetrahydro-4-oxo-1,5-benzothiazepin-3-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

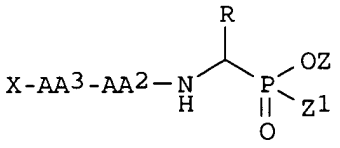
PAGE 1-A



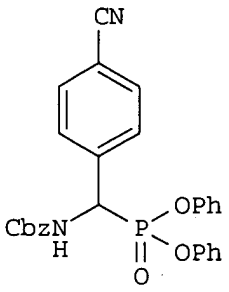


RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

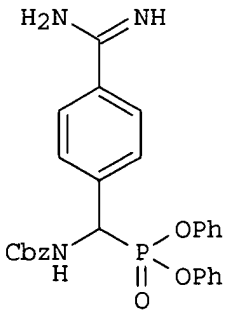
L4 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
GI



I



II



III

AB Peptidyl α-aminoalkylphosphonic acid diesters with basic substituents I [R = Ph, CH2Ph, C1-6 alkyl substituted with amidino, guanidino, isothioureido, or amino; Z = C1-6 perfluoroalkyl, Ph, Ph substituted with J; Z1 = C1-6 perfluoroalkyloxy, phenoxy, phenoxy substituted with J, C1-6 alkoxy, halo; J = halo, C1-6 alkyl, C1-6 perfluoroalkyl, C1-6 alkoxy, NO2, CN, OH, CO2H, amino, C1-6 alkylamino, C2-12 dialkylamino, C1-6 acyl, C1-6 alkoxycarbonyl, C1-6 alkylthio; AA2, AA3 = independently bond, blocked or unblocked D-, L-, or achiral amino acid residue; X = Y-CO, Y-SO2; Y = Ph-CH:CH, (2-furyl)CH:CH, (2-thienyl)CH:CH, (2-Pyridyl)CH:CH, 2-phenoxyphenyl, 3-phenoxyphenyl,

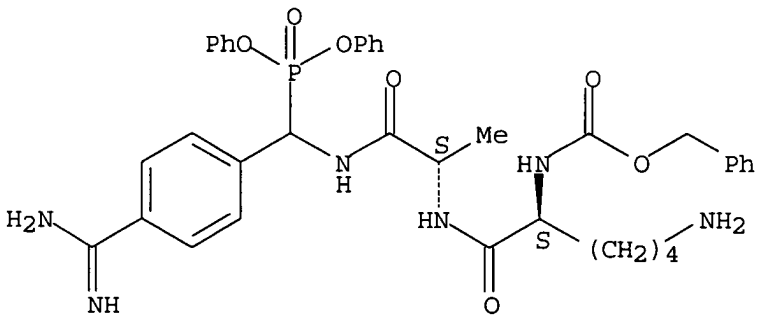
substituted Ph, C1-6 alkenyl substituted with a heterocyclic group, (un)substituted Ph, or (un)substituted naphthyl] and pharmaceutically acceptable salts thereof were prepared as compds. for use in inhibiting serine proteases with trypsin-like specificity and as anti-inflammatory agents, anticoagulants, and anti-tumor agents. Thus, condensation of 9.75 g 4-cyanobenzaldehyde with 7.65 g benzyl carbamate and 13.5 mL tri-Ph phosphite in 20 mL glacial acetic acid gave 70% cyanophenylphosphonate II. Amidation of II with ammonia and ammonium chloride in MeOH gave amidinophenyl derivative III as its HCl salt. III and related compds. were tested for inhibition of a variety of serine proteases.

AN 1999:582644 CAPLUS
DN 131:214554
TI Preparation of basic α-aminoalkylphosphonate derivatives as serine protease inhibitors
IN Powers, James C.; Jackson, Delwin S.; Ni, Liming
PA Georgia Tech Research Corp., USA
SO U.S., 18 pp., Cont.-in-part of U.S. 5,686,419.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5952307 | A | 19990914 | US 1997-907840 | 19970814 |
| | US 5686419 | A | 19971111 | US 1994-184286 | 19940121 |
| PRAI | US 1994-184286 | A2 | 19940121 | | |

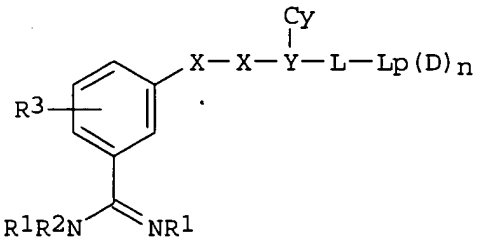
OS MARPAT 131:214554
IT **242817-08-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of basic α-aminoalkylphosphonate derivs. as serine protease inhibitors)
RN 242817-08-9 CAPLUS
CN L-Alaninamide, N2-[(phenylmethoxy)carbonyl]-L-lysyl-N-[[4-(aminoiminomethyl)phenyl](diphenoxyphosphinyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

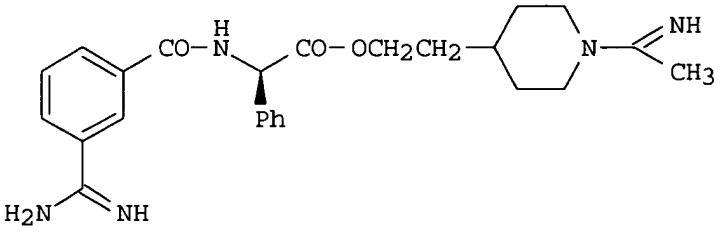



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
GI



I



II

AB Title compds. I [R1, R2 = H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl, cycloalkyl; R3 = R1, R2, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulfonyl, alkylsulfenyl, alkylsulfonamido, alkylaminosulfonyl, haloalkoxy, haloalkyl; X = C, N, O, S, CO, CR1, C(R1)2, NR1 with at least one X being C, CO, CR1 or C(R1)2, with the proviso that if the benzamidine group is unsubstituted and the X-X group is -CH2C(R1)2-, then R1 = H or attached to the alkylene carbon atom by a heteroatom; L = organic linker containing 1-5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Y = N, CR1; YL = cyclic group; Cy = (un)saturated, (poly)cyclic, (hetero)cyclic group optionally substituted by groups R3 or Ph optionally substituted by R3; Lp = lipophilic alkyl, heterocyclic, alkenyl, alkaryl, (poly)cycloalkyl, cycloalkenyl, aryl, aralkyl, haloalkyl, or a combination of two or more such groups optionally substituted by oxa, oxo, aza, thio, halo, amino, hydroxy or by R3; D = H bond donor group; n = 0-2] and their physiol. tolerable salts were prepared as serine protease inhibitors useful as antithrombotic agents. Synthesis methodol. for preparing some I was provided, and common starting materials were Fmoc- or Boc-(D)-phenylglycine and m-amidinobenzoic acid. Descriptions of enzyme assays were given, but no enzyme inhibition data was provided for I. To measure the antithrombotic activity, a partial thromboplastin time test assay was done, and for example, m-amidinobenzoyl-D-phenylglycine ester II (preparation not given, but 1H NMR characterization data provided), at 1.9 μM concentration, doubled the clotting time.

AN 1999:184269 CAPLUS

DN 130:237884

TI Preparation of meta-benzamidine derivatives of amino acids or dipeptides as serine protease inhibitors

IN Liebeschuetz, John Walter; Wylie, William Alexander; Waszkowycz, Bohdan; Murray, Christopher William; Rimmer, Andrew David; Welsh, Pauline Mary;

Jones, Stuart Donald; Roscoe, Jonathan Michael Ernest; Young, Stephen Clinton; Morgan, Phillip John
PA Proteus Molecular Design Ltd., UK
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 13

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9911658 | A1 | 19990311 | WO 1998-GB2605 | 19980828 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9888757 | A1 | 19990322 | AU 1998-88757 | 19980828 |
| | EP 1009758 | A1 | 20000621 | EP 1998-940430 | 19980828 |
| | R: DE, FR, GB, IT | | | | |
| | US 2002055522 | A1 | 20020509 | US 2001-988082 | 20011119 |
| | US 6740682 | B2 | 20040525 | | |
| | US 2003216403 | A1 | 20031120 | US 2003-296245 | 20030514 |
| | US 2004143018 | A1 | 20040722 | US 2004-752568 | 20040108 |
| PRAI | GB 1997-18392 | A | 19970829 | | |
| | GB 1998-3173 | A | 19980213 | | |
| | WO 1998-GB2605 | W | 19980828 | | |
| | GB 1999-13823 | A | 19990614 | | |
| | US 1999-142064P | P | 19990702 | | |
| | US 2000-485678 | A2 | 20000225 | | |
| | WO 2000-GB2291 | A2 | 20000613 | | |
| | WO 2001-GB2566 | W | 20010612 | | |
| | US 2001-988082 | A1 | 20011119 | | |

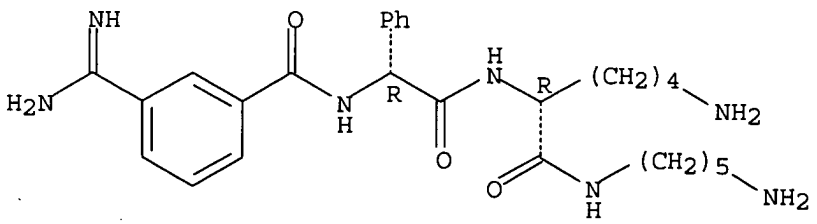
OS MARPAT 130:237884

IT **221232-83-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of meta-benzamidine derivs. of amino acids or dipeptides as serine protease inhibitors)

RN 221232-83-3 CAPLUS

CN D-Lysinamide, (2R)-N-[3-(aminoiminomethyl)benzoyl]-2-phenylglycyl-N-(5-aminopentyl)- (9CI) (CA INDEX NAME)

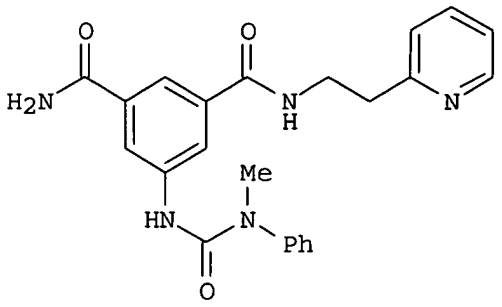
Absolute stereochemistry.



4/28/05

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
GI



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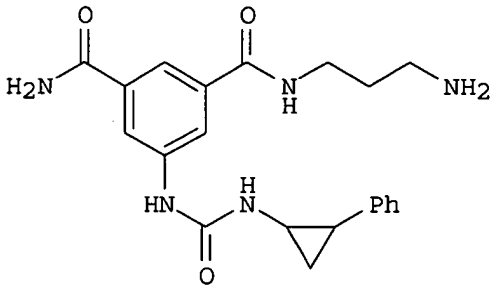


II

AB The invention provides a library of compds. containing a common animobenzenedicarboxylic acid core structure (scaffold) which serves as a template for synthesizing approx. 101-106 compds. which are analogs of the scaffold. The library is employed to study ligand binding by biol. receptors, such as enzymes, G-protein coupled receptors and membrane channels. For example, certain individual compds. within the library selectively bind and inhibit the action of trypsin-like serine proteases (no data). The invention also provides combinatorial synthetic methods for making such libraries. Addnl., the invention relates to novel scaffold-modified solid supports, especially resins, and methods for preparing them. Further, the invention is directed to screening methods, which comprise use of the compds. in suitable pharmaceutical assays. For instance, an FMOC-protected Rink amide MBHA resin was deprotected, coupled with mono-Me 5-nitroisophthalate as a scaffold precursor, and reduced with SnCl2 to give an amino ester resin. This was submitted to a sequence of reaction with triphosgene, amination to give a urea, ester hydrolysis, acid activation, amidation, and CF3CO2H clip. One obtained sublibrary (14 compds.) included compds. I and II.

AN 1998:394320 CAPLUS

DN 129:54189

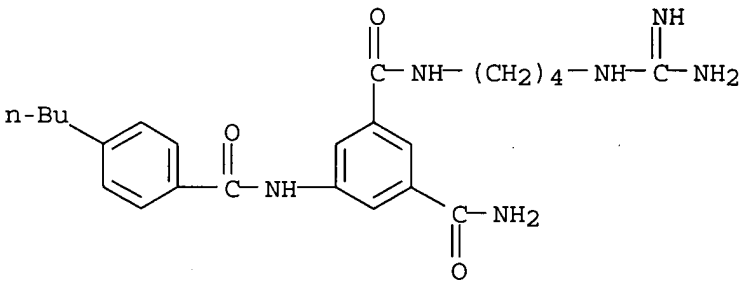
TI Aminobenzenedicarboxylic acid-based combinatorial libraries for discovery of protease inhibitors

IN Graybill, Todd L.; Wu, Zhengdong; Subasinghe, Nalin; Fedde, Cynthia L.; Salvino, Joseph M.

PA USA
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

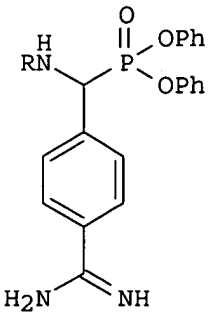
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9824760 | A1 | 19980611 | WO 1997-US21648 | 19971126 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9876242 | A1 | 19980629 | AU 1998-76242 | 19971126 |
| US 6127191 | A | 20001003 | US 1997-980062 | 19971126 |
| PRAI US 1996-32284P | P | 19961203 | | |
| WO 1997-US21648 | W | 19971126 | | |

OS CASREACT 129:54189; MARPAT 129:54189
IT **208756-58-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminobenzenedicarboxylic acid-based combinatorial libraries for discovery of protease inhibitors)
RN 208756-58-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[4-[(aminoiminomethyl)amino]butyl]-5-[(4-butylbenzoyl)amino]- (9CI) (CA INDEX NAME)




RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
GI



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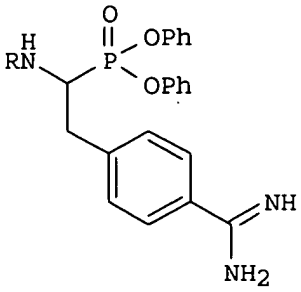


II

AB Thirty-six new amino acid and peptidyl phosphonate esters, e.g. I [R = PhCH2O2C (Cbz), HO2CCH2CH2CO (Suc), R1CH:CHCO, 3-PhOC6H4CO, 2-PhOC6H4CO, 1-C10H7SO2, 1-C10H7CH2O2C, Cbz-X, R2-Pro, Suc-Ala-Ala, Boc-D-Phe-Pro, PhCH2SO2-Gly-Pro; R1 = Ph, 2-furyl, 2-thienyl, 3-pyridyl; X = Ala, Val, Leu, Pro, Thr, Lys, Phe, Ala-Ala, Pro-Ala, Asp-Ala, Asp(OCMe3)-Ala, Lys-Ala, Lys(Boc)-Ala, Phe-Ala, Ala-Ala-Ala; R2 = 2-PhOC6H4CO, 3-PhOC6H4CO, Ph2CHCH2CO, PhCH2CH2CO; Boc = Me3CO2C] were synthesized and evaluated to identify potent and selective inhibitors for four trypsin-like proteases: lymphocyte granzymes A and K, human mast cell tryptase, and pancreatic trypsin. Among five Lys and Arg homologs, II (R = Cbz) is the most potent inhibitor for granzyme A, and CbzNHCH(PO3Ph2)(CH2)4NH2.HCl (III) is the best inhibitor for granzyme K, mast tryptase, and trypsin. Generally, phosphonates I inhibit granzyme A and trypsin more potently than granzyme K and tryptase. Dipeptide phosphonates I (R = Cbz-Ala, Cbz-Thr) are the most potent inhibitors for granzyme A, and I (R = Cbz-Thr) (kobs/[I] = 2220 M-1 s-1) was quite specific with much lower inhibition rates for granzyme K and trypsin (kobs/[I] = 3 and 97 M-1 s-1, resp.) and no inhibition with tryptase. The most effective inhibitor of granzyme A was I (R = PhCH2SO2-Gly-Pro) with a second-order rate constant of 3650 M-1 s-1. The most potent inhibitor for granzyme K was I (R = Ph2CHCH2CO-Pro) with a kobs/[I] = 1830 M-1 s-1; all other phosphonates inhibited granzyme K weakly (kobs/[I] < 60 M-1 s-1). Human mast cell tryptase was inhibited slowly by these phosphonates with III as the best inhibitor (kobs/[I] = 89 M-1 s-1). The overall results suggest that scaffolds of II (R = Phe-Thr) and Phe-Pro-Lys will be useful to create selective phosphonate inhibitors for granzymes A and K, resp., and that P4 substituents offer opportunities to further enhance selectivity and reactivity.

AN 1998:338712 CAPLUS
DN 129:95705

TI Synthesis and Evaluation of Diphenyl Phosphonate Esters as Inhibitors of the Trypsin-like Granzymes A and K and Mast Cell Tryptase

AU Jackson, Delwin S.; Fraser, Stephanie A.; Ni, Li-Ming; Kam, Chih-Min; Winkler, Ulrike; Johnson, David A.; Froelich, Christopher J.; Hudig, Dorothy; Powers, James C.
CS School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA, 30332-0400, USA

SO Journal of Medicinal Chemistry (1998), 41(13), 2289-2301
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English

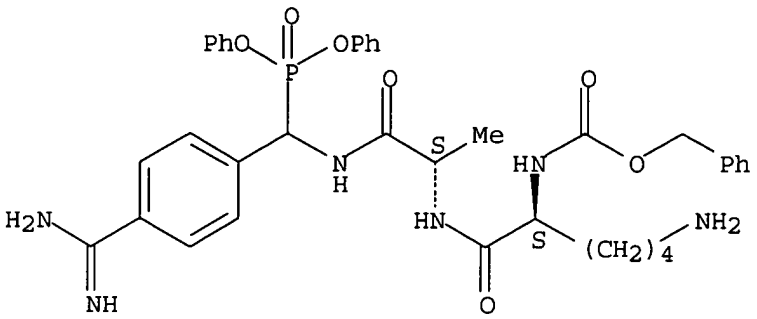
IT **209676-19-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity of phosphonate ester inhibitors of the trypsin-like granzymes A and K and mast cell tryptase)

RN 209676-19-7 CAPLUS

CN L-Alaninamide, N2-[(phenylmethoxy)carbonyl]-L-lysyl-N-[[4-(aminoiminomethyl)phenyl](diphenoxyphosphinyl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

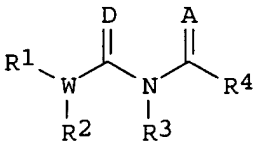


● HCl

RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

GI



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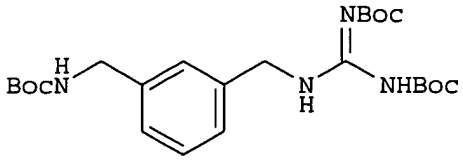
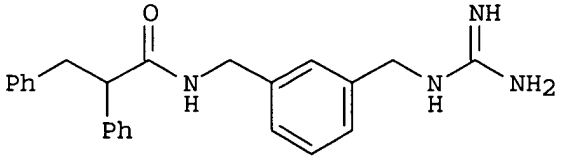
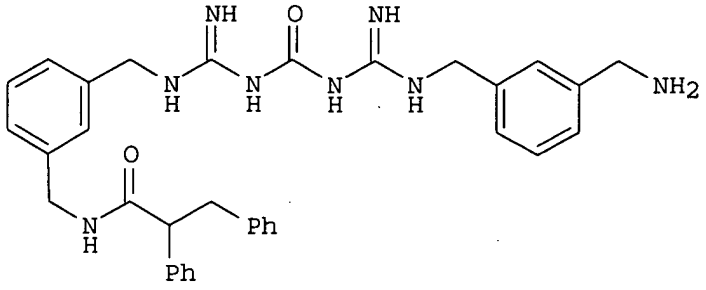


II



III



IV

AB Novel neuropeptide Y ligands I [A = O, S, NR; R = C1-8 alkyl; D = O, S, NR7, W = N, CH, CR8; R1, R3 = independently H, (un)substituted, straight or branched, cyclic or acyclic saturated or unsatd. C1-14 alkyl; R2 = Q(X3)-NR5-W2-R6; W2 = CO, SO2, CONH, S(O), bond; Q = (un)substituted (CH2)z, (CH2)m-Q1-(CH2)l, z = 1-12; when z >1, 1 or more CH2 groups may be replaced by O, S, or substituted N; l, m = independently 0-5; Q1 = C3-12 (un)saturated carbocyclic or heterocyclic ring; X3 = H, C1-8 alkyl, aryl, C1-8 alkoxy, OH, CF3, etc.; R4 = NR9R10, NR11-C(:A1)-NR9R10; A1 = O, S, NH, R12; R12 = H, C1-8 alkyl, aryl; R5-R9, R11, R12 = independently any group R1, aryl, heteroaryl; R10 = H, straight or branched, cyclic or acyclic, saturated or unsatd. C1-12 alkyl, (un)substituted aryl, aryloxyalkyl, 2- or 3-tetrahydrofurfuryl, (CH2)2-12-OH, amidoalkyl; NR9R10 = 3-10-membered ring], pure or partially separated stereoisomers or racemic mixts. thereof, free bases or pharmaceutically acceptable derivs. thereof, are disclosed. Compds. I are agonists and antagonists of neuropeptide Y, and are therefore useful as regulators of neuropeptide Y activity and in treating disorders related thereto. Thus, condensation of protected guanidine II (Boc = CO2CMe3) [prepared from 1,3-bis(aminomethyl)benzene and 1-(N,N'-di-Boc-amidino)pyrazole] and free guanidine III (prepared from II and 2,3-diphenylpropionylxb56 chloride), followed by deprotection, gave desired bis(amidino)urea IV. Compound IV inhibited binding of radiolabeled neuropeptide Y to cloned cell line receptors with IC50 = 70 nM.

AN 1998:147199 CAPLUS
DN 128:205146

TI Preparation of amidinourea derivatives as neuropeptide Y ligands

IN Gregor, Vlad Edward; Hong, Yufeng; Ling, Anthony Lai; Tompkins, Eileen Valenzuela
PA Agouron Acquisition Corp., USA; Gregor, Vlad Edward; Hong, Yufeng; Ling, Anthony Lai; Tompkins, Eileen Valenzuela

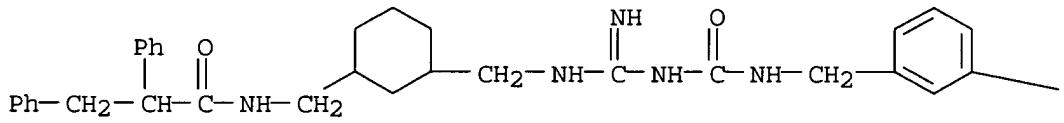
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9807420 | A1 | 19980226 | WO 1997-US14854 | 19970822 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2268051 | AA | 19980226 | CA 1997-2268051 | 19970822 |
| | AU 9741592 | A1 | 19980306 | AU 1997-41592 | 19970822 |
| | EP 984778 | A1 | 20000315 | EP 1997-939524 | 19970822 |
| | EP 984778 | B1 | 20020612 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | JP 2001502296 | T2 | 20010220 | JP 1998-511019 | 19970822 |
| | AT 218859 | E | 20020615 | AT 1997-939524 | 19970822 |
| | ES 2176776 | T3 | 20021201 | ES 1997-939524 | 19970822 |
| | US 6849733 | B1 | 20050201 | US 1997-916527 | 19970822 |
| PRAI | US 1996-25791P | P | 19960823 | | |
| | WO 1997-US14854 | W | 19970822 | | |

OS MARPAT 128:205146
IT **204070-60-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidinourea and bisamidinourea derivs. as neuropeptide Y agonists and antagonists)
RN 204070-60-0 CAPLUS
CN Benzenepropanamide, N-[[3-[[[[[[[[3-(aminomethyl)phenyl]methyl]amino]carbonyl]amino]iminomethyl]amino]methyl]cyclohexyl]methyl]-α-phenyl- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

—$CH_2$—$NH_2$

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

AB Title compds. T-Z-CONHCH(CH2B)CO-Y-(CH2)nR [I; T = (un)substituted Ph, naphthyl, heteroarom., N, O, S, or T1TC2U; T1, T2 = (un)substituted Ph; U = H, alkoxy, OPh; Z = bond, O, NH, CH2, CH2CH2, CH2O, CH2NH; B = amidine-containing group; Y = O, NR1; R1 = H, (un)substituted alkyl, CH2Ph; n = 1-3; R = (un)substituted Ph], neuropeptide Y antagonists, were prepared Thus, (R)-R2NHC(:NH)NH(CH2)3CH(NHR3)CONHR4 [II; R2 = 2,2,5,7,8-pentamethylchroman-6-sulfonyl (Pmc); R3, = Fmoc; R4 = CH2C6H4CH2NHCO2CH2Ph-4] was prepared from Fmoc-D-Arg(Pmc)OH and 4-PhCH2O2CNHCH2C6H4CH2CONH2, Fmoc-deprotected, and diphenylacetylated, to give II (R2 = Pmc; R3 = COCHPh2; R4 = CH2C6H4CH2NH2-4), which was N-acetylated and deprotected to give II-trifluoroacetate (R2 = H; R3 = COCHPh2; R4 = CH2C6H4CH2NHAc-4). I showed activity as neuropeptide Y antagonists in both in vitro (at 10-8 to 10-5 M) and in vivo tests (at 0.001 to 10 mg/kg).

AN 1997:473595 CAPLUS

DN 127:81788

TI Preparation of amino acid derivatives as neuropeptide Y antagonists

IN Engel, Wolfhard; Eberlein, Wolfgang; Rudolf, Klaus; Doods, Henri; Wieland, Heike-Andrea; Willim, Klaus-Dieter; Entzeroth, Michael; Wienen, Wolfgang

PA Dr. Karl Thomae Gmbh, Germany

SO Ger. Offen., 117 pp.
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | DE 19544687 | A1 | 19970605 | DE 1995-19544687 | 19951130 |
| | CA 2238859 | AA | 19970605 | CA 1996-2238859 | 19961126 |
| | WO 9719911 | A1 | 19970605 | WO 1996-EP5222 | 19961126 |
| | W: CA, JP, MX, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | EP 885186 | A1 | 19981223 | EP 1996-941032 | 19961126 |
| | EP 885186 | B1 | 20030326 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | JP 2000501390 | T2 | 20000208 | JP 1997-520166 | 19961126 |
| | AT 235459 | E | 20030415 | AT 1996-941032 | 19961126 |
| | US 6114390 | A | 20000905 | US 1997-950113 | 19971014 |
| PRAI | DE 1995-19544687 | A | 19951130 | | |
| | WO 1996-EP5222 | W | 19961126 | | |
| | US 1998-945048 | A | 19980210 | | |

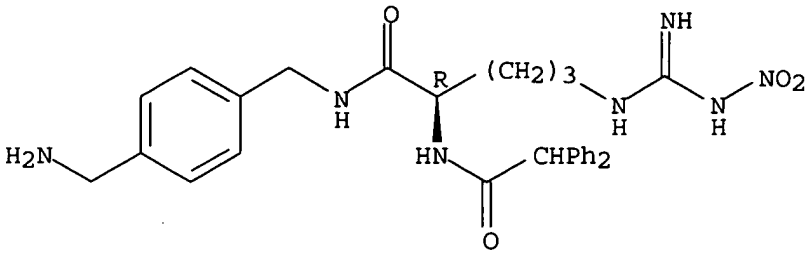
OS MARPAT 127:81788

IT **191869-48-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid derivs. as neuropeptide Y antagonists)

RN 191869-48-4 CAPLUS

CN Benzeneacetamide, N-[1-[[[[4-(aminomethyl)phenyl]methyl]amino]carbonyl]-4-[[imino(nitroamino)methyl]amino]butyl]-α-phenyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.


O
NH
R
(CH2)3
NO2
N
H
N
H
N
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H2N
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CHPh2
O